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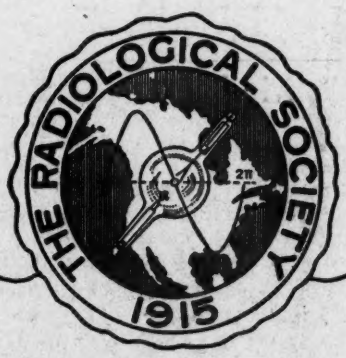

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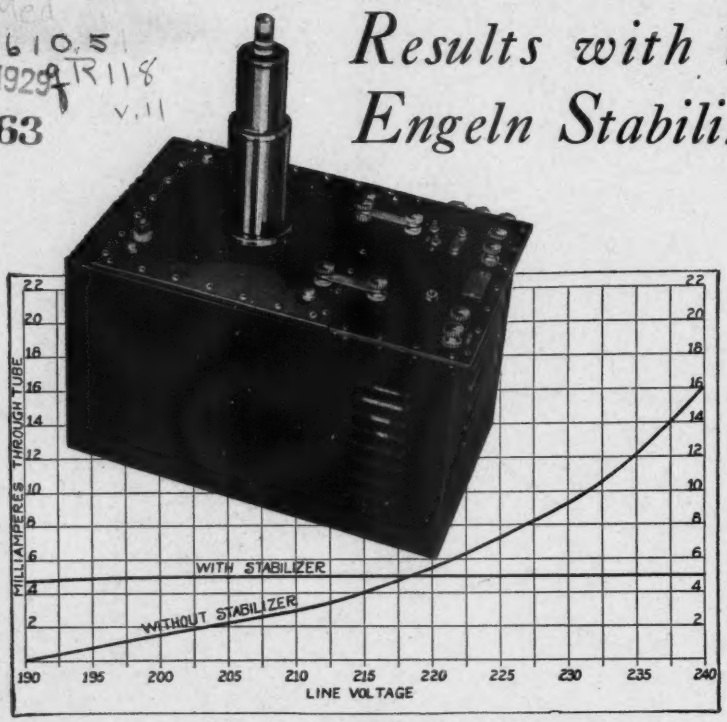

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VOL. XI JULY, 1928 No. 1

SOME PSEUDO-VESICULAR SHADOWS AND OTHER PITFALLS IN GALL-BLADDER ROENTGENOLOGY[1]

By JAMES T. CASE, M.D., F.A.C.S., D.M.R.E. (Camb.); Surgeon, Battle Creek Sanitarium; Professor of Roentgenology, Northwestern University Medical School (Chicago), BATTLE CREEK, MICHIGAN

IN the beginning of gall-bladder roentgenology, long before the introduction of the Graham test, it was not uncommon to observe in the films of the gall-bladder region an ovoid shadow corresponding rather closely in form and size to the gall bladder. It was natural to assume that this shadow was caused by the gall bladder, and numerous studies were made and papers written on the value of the gall-bladder shadow in the roentgenogram as a sign of gall-bladder disease.

It was rather generally supposed that if the gall bladder cast a shadow upon the roentgen film, it was because the gall bladder was pathological; and it was presumed that the normal gall bladder would not cast such a shadow. Care was taken to make sure that one was not mistaking the shadow of the liver or the kidney for this supposed gall-bladder shadow. It was soon established as a primary requirement of a good gall-bladder region film that the outline of the kidney and the shadow of the lower border of the liver should both be distinctly recognizable; and, if a third rounded shadow was recognized, it was assumed to represent the gall bladder. On the basis of this assumption, not a few erroneous diagnoses of gall-bladder disease have been made. Indeed, in a considerable proportion of films, more than one such ovoid shadow was visible, and one was put to it to select the shadow to be called the gall-bladder outline.

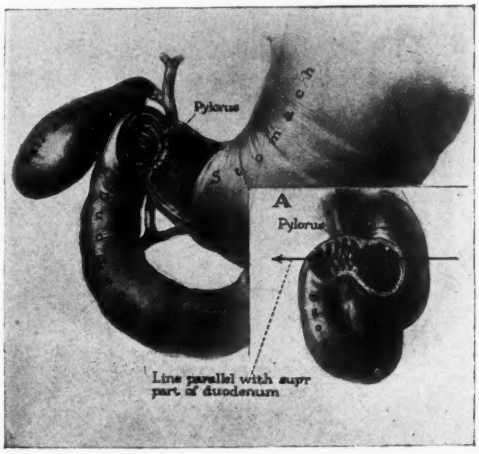

Fig. 1. Diagram illustrating the posterior direction taken by the duodenal bulb and the upper part of the second portion of the duodenum. Note how the shadow of the duodenal wall is for a considerable distance seen in profile, thus giving most favorable conditions for casting an ovoid shadow, oftimes imprisoning a small quantity of gas.

It was not difficult to acquire statistics favoring the value of the supposed gall-bladder shadow as a sign of gall-bladder disease, for naturally only such cases as had

[1]Presented before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

Fig. 2. Arrows on reader's right point to an ovoid shadow believed to be cast by the duodenum. Note the visualized, stone-filled gall bladder, lying to the outer side of this duodenal shadow (on the reader's left, marked "G"). Note gas imprisoned in duodenum.

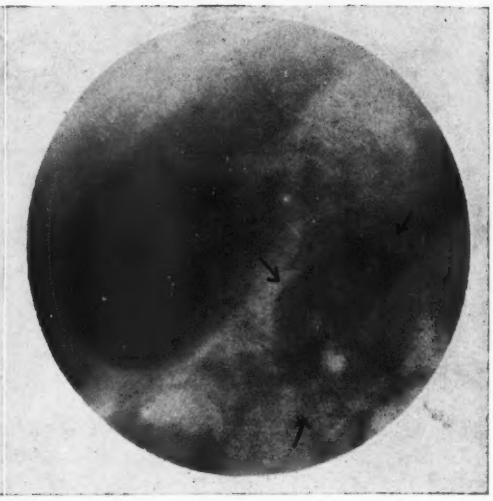

Fig. 3. Another instance of an ovoid shadow (shown by arrows) in the right upper quadrant, due to the duodenum. Gall bladder, visualized by tetraiodophenolphthalein, shown at the outer side of the duodenal shadow. Note gas within duodenal shadow.

at least a reasonable amount of clinical confirmation of the tentative diagnosis where likely to come to surgery. The writer has seen scores of cases exhibiting this supposed gall-bladder shadow in which no surgical confirmation was obtainable because there were no clinical signs of gall-bladder disease. It is a fact that in a series of operations for

Fig. 4. Shows two shadows: "a," which is the distorted gall bladder visualized by cholecystography; "b," a somewhat larger elliptical shadow erroneously considered to be the gall bladder before the Graham test was administered (see Figure 5).

Fig. 5. (Compare with Figure 4.) The barium-filled stomach, the pyloric end of which undoubtedly caused the shadow "b" in Figure 4, made before the opaque meal was administered.

Fig. 6. Another illustration of two shadows: one, the gall-bladder shadow, visualized by cholecystography; the other faint shadow (indicated by three arrows) cast by the pyloric end of the stomach before the administration of the opaque meal (see Figure 7).

Fig. 7. (Compare with Figure 6.) The pyloric end of the stomach corresponding to the faint shadow indicated by three arrows in Figure 6.

definite gall-bladder disease, a certain proportion of the cases will have shown this ovoid shadow. This fact led various observers to conclude that the pathologic gall bladder should cast a shadow discernible on properly exposed and developed films. Indeed, several qualitative and quantitative estimations have been made of the bile present in such gall bladders, and microscopic studies have been made of sections of the vesical wall, in the effort to determine if and why the pathologic gall bladder should cast a shadow and the normal gall bladder should not.

In an attempt to explain this often misleading shadow, the writer, in a discussion before the American Roentgen Ray Society, in September, 1922, offered the following explanation, believing that both normal and pathologic gall bladders could be portrayed in shadow on the roentgen film. It will be recalled that in the early days of roentgenology of the kidney, exposures were so prolonged that the kidney shadow was not seen on the roentgenogram and the shadow of stones was frequently blurred. With improvements in apparatus and technic, we began to see the outline of the kidney; and several authors seriously suggested that when the kidney outline was discernible on the film, it was because of tuberculous disease. It was not long, however, before general recognition was given the fact that no roentgenogram was suitable for diagnostic purposes unless it clearly showed the outline of the kidney. The writer therefore suggested that this might be true also of the gall bladder, and that this supposed outline of the gall bladder was seen on certain films, even under normal conditions, not because of a denser gall bladder, but because of better technic. This partially explains the occurrence of the shadow, but, as will be seen below, the shadow in question may be due to other causes than the gall bladder.

With the introduction of cholecystography three years ago by Graham and his associates, it at once became evident that many of these shadows which we had previously supposed to represent the gall blad-

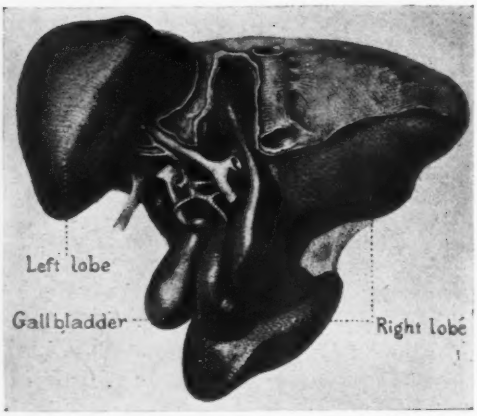

Fig. 8. Illustration, borrowed from Thomas S. Cullen, showing the under surface of a markedly lobulated liver with three very similar outlines, having the same general size and shape as the gall bladder. One is the gall bladder; the other two are accessory lobes of the liver.

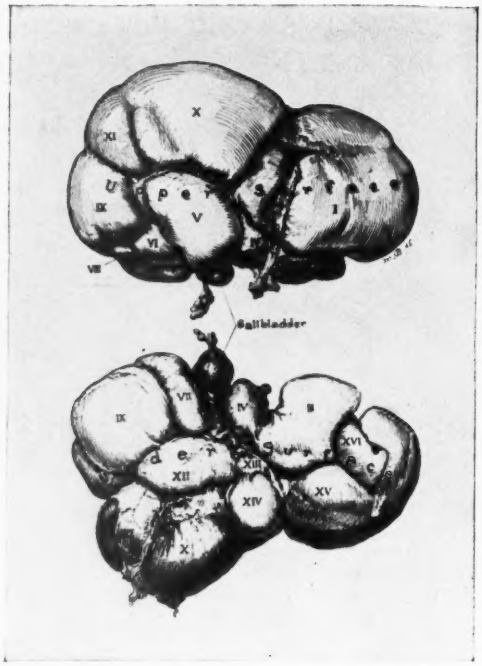

Fig. 9. Another illustration borrowed from Cullen showing the anterior and posterior aspects of the liver, the gall bladder being plainly marked. Note the numerous other lobes closely resembling the gall bladder in size and shape. The original drawing was presented by W. Moser (Med. Rec., 1898, LIII, 672).

der, were not due to the gall bladder at all; for the shadow of the dye-filled gall bladder was seen to be separate and distinct from, and usually lying to the right of, the ovoid shadow under discussion. It was, therefore, apparent that we had previously been mistaken as to the identity of the ovoid shadow formerly supposed to be due to the gall bladder. True enough, in certain instances we had reason to believe that this shadow was due to the gall bladder itself, for we sometimes saw gallstones occupying the middle of this shadow, thus identifying it quite circumstantially; but that we had been mistaken in a large percentage of the cases was soon quite evident to every one doing cholecystography.

The writer now suggests that this ovoid pseudo-vesicular shadow may be due in certain instances, probably in most, to one of the following causes:

(*a*) The shadow of the bulb and upper portion of the second part of the duodenum itself where the duodenum passes posteriorly to make the beginning of the duodenal curve. The average roentgenogram of the abdominal region shows the psoas muscles, for instance, and even the lumbar muscles, and a number of other outlines which can be delineated on a well exposed film; and it is reasonable to suppose that at times we may see a rounded shadow just below the inferior border of the liver due to the "piled up" shadow of segments of the duodenum in profile. In support of this suggestion is the fact, well noted by many observers, that quite often one sees within this supposed gall-bladder shadow a collection of gas having the characteristic outline of the interior of the small intestine, due, we believe, to the imprisonment of a small amount of gas or air in the duodenal bulb or first part of the descending portion of the duodenum. Figure 1 explains this suggestion.

Figures 2 and 3 illustrate the rounded pseudo-vesicular shadows, which, in our opinion, are caused by the duodenum.

(*b*) The pyloric end of the stomach may cause a pseudo-vesicular shadow, although it is likely to be larger than one would expect for the outline of the gall bladder. Figures 4, 5, 6, and 7 illustrate such a pseudo-gall-bladder shadow.

(*c*) In other instances, a pseudo-gall-bladder shadow may be caused by enlargement of the lobus Spigelii of the liver, as was suggested by the writer in 1913 (1). Reference to any text-book on anatomy will reveal the fact that the liver lobes are by no means constant in form or size. Figures 8 and 9 are illustrations from Dr. Thomas S. Cullen's article, "Accessory Lobes of the Liver" (2), showing unusually formed lobes. It is easy for the roentgenologist to understand how in a patient having such a liver we might in one or more films of the gall-bladder region succeed in recording an ovoid pseudo-vesicular shadow.

A further proof, most convincing of all, that these ovoid right upper quadrant shadows lie outside of the liver and kidney or at least often are not due to the gall bladder, is the fact that we have in many instances been able to demonstrate them on films of patients who have had the gall bladder removed. *With rare exceptions, the writer deems it impossible with surety to identify any right upper quadrant rounded or ovoid shadow as due to the gall bladder until the gall bladder has been visualized by the ingestion or injection of dye by the Graham-Cole method.*

Another interesting fact which we have come to recognize since the introduction of cholecystography is the error of some of our former doctrines concerning the so-called gall-bladder impression on the shadow of the duodenum. We formerly taught that when the duodenal bulb was constantly deformed, the lesion was usually an organic one, and, in the great majority of instances, due to an ulcer; but when the deformity of the duodenal bulb was inconstant, depending upon the position of the patient, we frequently observed a misshapen outline suggesting compression by some ovoid organ, corresponding very accurately in size and shape to our conception of the gall bladder (Fig. 10). This supposition was still further strengthened by the fact that in numerous instances we have been able to demonstrate gallstones in such relation to this deformed duodenal bulb that it seemed that they were contained within the gall bladder and that therefore it was the gall bladder that made this impression in the duodenal bulb. However, we fre-

Fig. 10. A so-called "gall-bladder impression" in the duodenal bulb, formerly thought to be due to the gall bladder, but which, in the light of facts advanced in this article, may undoubtedly be due to other causes.

quently noted this so-called gall-bladder impression in the duodenal bulb in cases where we had no clinical reason to suspect gall-bladder disease; and sometimes, when the patient came to surgery for some other reason, we were able to demonstrate definitely that in many of these cases the gall bladder was not diseased.

The same reasoning which has led us to doubt the correctness of our supposition of the pre-Graham days that we were actually visualizing the gall-bladder outline, leads us to offer the same explanation for this so-called "gall-bladder impression" upon the duodenum. Although sometimes truly due to the gall bladder, this impression may just as well be due to the Spigelian lobe of the liver, or some other usual or unusual lobe of the liver, as to the gall bladder. Our cholecystographic studies made simultaneously with the opaque meal lead us to believe that very often the gall-bladder shadow may be deformed by pressure of the duodenum. The time has come, in fact, when we may just as well talk of the duodenal impression upon the gall bladder as of the gall-bladder impression upon the duodenum. Possibly if the Graham test had been devised before the opaque meal, all these years we would have been talking about the duodenal impression on the gall bladder. It is not clear that either impression signifies a pathological situation. The important thing is to recognize the cause of the impression and to realize that the deformed duodenal bulb which we have hitherto thought significant of gall-bladder disease may be due to pressure of a liver lobe and not to pression from the gall bladder itself.

SUMMARY

1. In the direct examination of the gall bladder without the aid of cholecystography, a small, rounded, ovoid shadow in the right upper quadrant, distinctly not caused by the inferior border of the liver or the kidney, is in all probability due to something else than the gall bladder.

2. This statement is borne out by the fact that such an ovoid shadow may appear even in patients from whom the gall bladder has been removed; and by the further proof that the gall bladder visualized by the Graham method generally does not coincide with this ovoid shadow, formerly supposed to represent the gall bladder.

3. This ovoid shadow is usually due (*a*) to "piling up" of the shadow of the first portion of the duodenum, or (*b*) to an unusual (perhaps even usual) arrangement of one of the smaller lobes of the liver, or (*c*) to the shadow of the pyloric end of the stomach, even without resorting to an opaque meal.

4. The same explanations apply to the rounded so-called "gall-bladder impression" of the first part of the duodenum, formerly thought to be due to pressure of the gall bladder.

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CHOLECYSTOGRAPHY[1]

AN ANALYSIS OF 1,500 CHOLECYSTOGRAPHIC EXAMINATIONS WITH CORRELATED CLINICAL AND LABORATORY FINDINGS, WITH SPECIAL REFERENCE TO PERNICIOUS ANEMIA, MYOCARDIAL DEGENERATION, INFECTIOUS ARTHRITIS, AND GASTRIC ACID CONTENT

By I. H. LOCKWOOD, M.D., and E. H. SKINNER, M.D., KANSAS CITY, MISSOURI

THE keystone of the practice of medicine is diagnosis. Diagnosis consists of carefully and orderly made observations, correctly associated, soberly evaluated and then intelligently deducted. The average diagnosis is not all that is to be desired by any means and this is brought home by the revelation made at autopsy. It has been demonstrated that not only do we often fail in identifying the actual primary lesion but with appalling frequency we entirely miss the complications that are present. With the known high incidence of disease of the gall bladder we have been glad to promote a more accurate method of studying the biliary tract. Before the development of cholecystography, as advanced by Graham, Cole, Copher, and Moore (1), roentgen examination of the gall bladder consisted in the demonstration of stones, a thickened gall-bladder wall, and a few indirect signs of cholecystic disease. When these signs are elicited any one or all of them are of the greatest value in enabling one to arrive at a correct conclusion in regard to the existence of disease in the biliary tract. Unfortunately these findings are, at best, difficult to elicit, allow of uncertainty in interpretation and difference of opinion, and—most serious drawback of all—are not inevitable signs of disease of the gall bladder. They may be, and frequently are, entirely lacking in extreme cholecystic disease, even of chronic nature. Their existence is probably always a sequence to long-standing or repeated attacks of gall-bladder disease and never of its acute phases.

Cholecystography seems to bridge the gap left by the older methods of roentgen examination and supplies a much more precise knowledge of the diseased gall bladder. Although cholecystography has given so much, and the promises of the future are so great, there are no indications that it will supplant the older methods of examination in this field. Instead of simplifying the procedure it has complicated it by introducing another step that has to be carried out, if the best type of work is to be done. This added complexity, however, is offset by the value of the findings obtained.

We do not believe that the patient with symptoms of gall-bladder disease should have the investigation of the gastro-intestinal tract omitted. The best results will be obtained by direct roentgen examination of the gall bladder, a gastro-intestinal examination, and cholecystography.

In a series of 1,500 cases we have given the dye by oral administration. Our method of employing cholecystography has remained essentially the same and there has been no significant change in our ideas regarding interpretation of the cholecystogram. We have followed a very definite technic in the preparation of the patient. Plain negatives made in two projections have preceded the administration of the dye. On the day the capsules were to be administered a cleansing enema was given with a noon meal rich in fats and cream. At 6 P. M. nothing but tea and toast without butter or cream was allowed. The capsules were given at 8 P. M. in four doses 15 minutes apart, the patient being cautioned not to break the capsule in the mouth. Twenty grains of sodium carbonate had

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

been taken just before the capsules. In the smaller individuals we have given an approximate dose of 1 grain for each 5 pounds of body-weight; in the heavier individuals 1 grain for each 4 pounds of weight. Patients were asked to refrain from taking food the following morning. We feel it is very essential not only to refrain from food but the odor of food as well.

We have found no contra-indications for the oral administration of the dye, unless it be in the individual whose condition is so serious as to make any similar procedure dangerous. In none of our cases has there been any significant change in pulse, respiration, or blood pressure following administration of the dye. We have given it to patients with myocardial degeneration without any reaction. Electrocardiograms taken before and after the administration have shown no change in any of its leads. In no case has the urine shown albumin, sugar, red blood cells or casts following its administration. We have given the dye to pregnant women and obtained excellent shadows without adverse symptoms. We have also given it to nursing mothers and none of them have shown any reaction. The infants have been allowed to nurse and none have shown diarrhea, colic or any other upset of the gastro-intestinal tract.

In this series of 1,500 cases, with the dye given orally, 610 have been considered pathologic, the remainder normal. Of these 610 pathologic cases, 278 presented no shadow of the dye in the gall bladder. Of the total number of pathologic cases 192 have been operated upon and in only 7 instances has an incorrect pre-operative opinion been shown to have been given, a percentage of 96.4 correct findings following gall-bladder surgery. In two of our no-shadow cases the X-ray findings were indicative of a carcinomatous involvement of the pyloric end of the stomach, obstructive in type. These two cases, when operated upon, disclosed normal gall bladders. The capsules in one of these cases remained in the stomach longer than 72 hours: at the end of this time only three of them had broken down. The other case showed the capsules remaining in the stomach at the end of 36 hours, about one-half of them having disintegrated. The interesting factor in both of these cases was that there was no vomiting, no nausea, no diarrhea or any adverse symptoms. A third no-shadow case at operation revealed a carcinoma of the mid-portion of the transverse colon. The four other cases in which an erroneous opinion was given showed very poor concentration of the dye in the gall bladder. We felt that we were dealing with a definite thickening of the gall-bladder walls and an extremely poor concentration function. In these four cases the surgeon and pathologist tell us that there was no evidence of any pathologic changes in the walls of the gall bladder. The three cases of malignancy undoubtedly should never have had the visualization done. We have included them in this correlation because of the consecutive run of the cases. Undoubtedly pyloric obstruction is a contra-indication to the use of the dye by oral administration. In 176 of these cases stones were found. Stones were also found in 112 of the no-shadow cases. The remainder were either the cholesterin type of stones or calcium stones in a gall bladder which visualized. In 168 cases either a flocculency or undissolved capsules appeared in the gastro-intestinal tract, including the two cases in which the capsules remained in the stomach for 36 and 72 hours, respectively. In all of our cases a negative has been made covering the entire gastro-intestinal tract.

Our 278 no-shadow cases have agreed with the clinical diagnosis in all but 6 instances. Two of these, referred to above,

had carcinoma in the pyloric end of the stomach; the third, carcinoma of the colon; fourth, a severe case of thyrotoxicosis with a large fibroid; fifth and sixth, two cases of syphilitic hepatitis.

That the amount of free hydrochloric acid (2) in the gastric secretion of a subject for cholecystography, where the dye has been given orally, acts as a factor in the intestinal reaction to the chemicals and influences the resulting cholecystogram in our experience seems to have no foundation. In this series of 1,500 cases, 126 have had diarrhea of a moderate type; 22 have had rather severe diarrhea; 162 have complained of nausea, but no vomiting; 154 have had nausea and vomiting; only three complained of headaches.

A gastric analysis including both the fasting and Ewald meal has been made in 1,024 of these cases; 524 have shown a normal visualization and 500 have been pathologic.

In the 524 cases with normal visualization the free hydrochloric acid in the fasting meal has been absent in 294 cases, between 1 and 25 in 107 cases, between 25 and 50 in 100 cases, between 50 and 75 in 60 cases, and between 75 and 100 in 19 cases. The total acidity in these cases has been between 1 and 25 in 306 cases, between 25 and 50 in 137 cases, between 50 and 75 in 60 cases, between 75 and 100 in 19 cases, and over 100 in 2 cases. In the Ewald meal the normal gall bladders have shown that the free hydrochloric acid is absent in 92 cases, between 1 and 25 in 222 cases, between 25 and 50 in 172 cases, between 50 and 75 in 35 cases, and between 75 and 100 in 3 cases. The total acidity in the Ewald meal has been between 1 and 25 in 90 cases, between 25 and 50 in 165 cases, between 50 and 75 in 192 cases, between 75 and 100 in 85 cases, and over 100 in 2 cases.

The pathologic gall bladders have shown that there has been an absence of free hydrochloric acid in the fasting meal in 305 cases, between 1 and 25 in 109 cases, between 25 and 50 in 72 cases, between 50 and 75 in 11 cases, and between 75 and 100 in 3 cases. The total acidity in the fasting meal in these pathologic gall bladders has been between 1 and 25 in 312 cases, between 25 and 50 in 104 cases, between 50 and 75 in 73 cases, between 75 and 100 in 9 cases, and over 100 in 2 cases.

In the Ewald meal the pathologic gall bladders have shown an absence of free hydrochloric acid in 110 cases, between 1 and 25 in 197 cases, between 25 and 50 in 170 cases, between 50 and 75 in 22 cases, and between 75 and 100 in 3 cases. The total acidity in the Ewald meal has been between 1 and 25 in 110 cases, between 25 and 50 in 118 cases, between 50 and 75 in 208 cases, and between 75 and 100 in 64 cases.

In our series the free hydrochloric acid apparently has had no effect upon the resulting cholecystogram or the alimentary reaction. With 56 per cent of the cases with normal cholecystograms there was an absence of free hydrochloric acid, while 61 per cent of the cases with pathologic gall-bladder findings showed an absence of free hydrochloric acid in the fasting meal. While the association of gall-bladder disease and achlorhydria is quite striking, the evidence has been much more pronounced in the frank pernicious anemia cases. We have had, in this series, 31 cases of pernicious anemia of which 22 gave pathologic cholecystograms and 12 had stones.

Jones and Joyce noted the association between gall-bladder disease and pernicious anemia and elaborated on the effects of gall-bladder operations in their pernicious anemia cases with definite cholecystographic evidence of disease. They speak of five border-line cases in their series. While possessing all the clinical symptoms and signs of pernicious anemia, these cases differ from the rest in that their anemia is not

quite so grave and that the general course is longer and not severe. They were unable definitely to classify their cases as distinct from true pernicious anemia. We have seen several such patients whose anemia has been very strikingly influenced by gall-bladder surgery as well as medical treatment. We, too, are unable to furnish data or methods whereby these cases can be separated from ordinary pernicious anemia, but are convinced that in certain cases of mild, so-called pernicious anemia, the infected gall bladder plays an important rôle. We have been struck by the fact that, in several individuals in whom we suspected the gall bladder as being important etiologically in the anemia, treatment with liver and ordinary measures was much more efficacious than in the other group.

In studying these gall-bladder cases we have gained the impression that there is a very distinct relation between gall-bladder disease and myocardial changes. Electrocardiograms have been made in 367 of the cases showing gall-bladder disease and 71 per cent have shown myocardial changes. In this series we have had three operative deaths, one patient dying on the operating table, the second a few minutes after leaving the operating room, and the third five days after operation. All three of these cases showed marked myocardial degeneration. A fourth case, in which the surgeon advised against operation because of the electrocardiographic findings, died within 24 hours after leaving the hospital.

Several cases have been seen in which the electrocardiogram and the gall-bladder visualization have differentiated the conditions of angina pectoris and gall-bladder disease. One case in which the patient had a bundle branch block and in whom the gall-bladder visualization was considered normal, had had Lyon-Meltzer drainage for several months, and, when treated for his heart condition, was promptly relieved of his symptoms.

Two other patients who came in for gall-bladder disease, both showing normal cholecystograms with the electrocardiograms revealing bundle branch block, died, one suddenly in the hospital and the other about two weeks after leaving the hospital.

INFECTIOUS ARTHRITIS

In this series of cases we have found 168 showing definite evidence of infectious arthritis. One hundred and eleven of these have shown pathologic cholecystographic findings and 24 cases have shown stones. Many of these cases have shown no other focus of infection and several have had all other foci removed, with the arthritis still remaining. Exceptionally good results have been obtained in a few cases operated upon.

COMMENT

In this series of cases, only 12 per cent of which were hospitalized, we feel that the oral administration of the dye has given very satisfactory results. We appreciate that there are many errors which may occur when giving the dye orally, but the lack of any serious reaction and the ease of conducting the examination certainly offset the bare chance of erroneous findings, especially if one is reasonably careful of his technic in preparation of the patient and takes into consideration the absorption of the dye from the intestines and its excretion from the liver, when interpreting the resulting cholecystogram.

The fact that the patient may have an achlorhydria or an excess of free hydrochloric acid in the gastric secretion in our experience has had no bearing upon the result.

Moore has frequently made the statement that cholecystography is a measure of the

ability of the gall bladder to concentrate the bile which enters it. This undoubtedly is the greatest value of cholecystography but we feel that another positive finding can be made that is of almost equal value, by giving the fat meal which will determine the reduction in size and musculative activity of the gall bladder. We have seen many cases with an apparent normal visualization that failed to contract and empty within the normal limits of time, that at operation showed definite adhesions to the walls of the gall bladder and resulting muscular change. This condition has been found many times in old infiltrative duodenal lesions.

The total absence of any concentrated gall-bladder shadow (4) should indicate a pathologic condition, but without the clinical symptomatology to corroborate these findings and negative X-ray studies of the gastro-intestinal tract, such failure of concentration should be subject to re-examination. We have re-examined 48 of our no-shadow cases and 12 of these have been re-examined the third time, without any change in the cholecystogram.

The cholecystographic findings have been marked in our 31 cases of pernicious anemia; 22 have shown pathologic gall bladders and 12 have revealed stones. We feel that it has been a valuable aid in determining a certain type of pernicious anemia and in our cases has been of prognostic value and also aided in determining the type of treatment to follow.

That there is a definite relation between gall-bladder disease and myocardial degeneration there is no question of doubt. With electrocardiographic findings on 367 cases with diseased gall bladders, 71 per cent show definite myocardial changes. We have also shown that there exist cases simulating gall-bladder disease with a resulting normal cholecystogram and definite electrocardiographic findings that are oftentimes treated for gall-bladder disease with failure.

Cholecystography is an aid in revealing one of the many foci in infectious arthritis. In 168 cases of infectious arthritis, 111 have shown a pathologic gall bladder and 24 have shown stones.

SUMMARY

1. Oral cholecystography in 1,500 cases, only 12 per cent hospitalized, has been most satisfactory. Re-examination in 48 cases failed to change findings.

2. The reduction of the filled gall bladder after a fatty meal may be regarded as an index of function.

3. Hyperchlorhydria or achlorhydria seem to offer no interference to obtaining good gall-bladder shadows.

4. The total absence of gall-bladder shadow requires clinical corroboration and negative barium meal findings.

5. In pernicious anemia, 70 per cent showed pathologic gall bladders, with 39 per cent showing stones.

6. In myocardial degeneration, 71 per cent showed gall-bladder pathology and definite electrocardiographic findings.

7. There are cases of myocardial degeneration with gall-bladder symptoms but normal cholecystographic findings.

8. Cholecystography reveals another focus of infectious arthritis. In the cases of infectious arthritis, 69 per cent showed pathologic gall bladders, with 15 per cent showing stones.

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DEVELOPMENT OF ROENTGENOLOGIC EXAMINATION OF THE BILIARY TRACT[1]

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OUR present civilization differs from the civilizations of the past chiefly because of its larger mastery of the forces of nature. This is manifest in medicine, particularly in the greater control of light. The control of light permits the utilization of the microscope, the various endoscopic devices, and the roentgenologic apparatus. With these mechanisms for employing light, it is obvious that discovery of the method of control has preceded the medical application and that the degree of control has imposed boundaries beyond which medical usage can not pass.

The development of roentgenology has been dependent upon the development of roentgenologic apparatus. The discovery itself came from the physical laboratory, and every roentgenogram is a silent tribute to the labors of von Guericke, the mayor of Magdeburg, who devised the air pump; to the Abbé Nollet, who passed electric discharges through partially exhausted globes; to Faraday and Geissler, and to the brilliant physicists of the latter part of the XIXth century—Crookes, Lenard, Hertz, Thomson, and others, as well as to Röntgen himself. The announcement of the discovery was attended by a widespread public interest which, insofar as I am aware, has not been paralleled by any other laboratory findings. Hering (1), writing a few weeks after the announcement from Würzburg, describes it as having "stimulated hosts of inquirers and imitators into a scientific scramble, the like of which has probably never before been seen. It has been like a rush to the gold fields, and might perhaps recall to a forty-niner some of the incidents of that eventful period of discovery." By way of prophecy he adds, "In this instance, too, as in that, it is probable that much of the final profit will be derived, not from the gold digging, but from such other interests as grow out of it." And since the early prospecting was done chiefly by the physicist, the electrician, the inventor, and the photographer, while the permanent mining has fallen largely to the physician, this prediction has been to a large extent verified. In the "Bibliography of X-ray Literature" by Phillips (2), dated 1896-97, but about 5 per cent of the articles listed have a medical bearing and of these less than one-third have appeared in medical periodicals. The apparent dearth of activity on the part of physicians at this time was undoubtedly due in considerable part to a lack of facilities. There were, however, a few who had both interest and opportunity, and of these at least two merit homage in connection with the development of the roentgenology of the gall bladder; one, Macintyre of Glasgow (3), was the first to demonstrate roentgenologically a renal calculus in a living person, thus presaging the visualization of gallstones by the same means, and the other, Williams of Boston (4), was probably the first to employ a contrast meal in observing the behavior of the human stomach, thus initiating a method that was later to have a wide application in the diagnosis of gall-bladder disease. In a broader way, too, the names of these men deserve recognition on account of their having been the foremost in their respective countries in transplanting the roentgen ray from the physical laboratory to the laboratory of the physician.

The first alliances of physicians interested in roentgenology seem to have been largely with university physicists. With the increase in demand for apparatus, commercial

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

firms rose to supply it, and since then roentgenologists and the manufacturers of roentgen apparatus—groups now mutually dependent upon each other for their existence, as such—have labored together in endeavoring to perfect the technical side of this specialty. In general, this symbiotic association has been a happy one, the one group constantly stimulating and aiding the other. That this connection has not been invariably serene is indicated by an incident related to me by a graduate of the University of Würzburg. He said that while working in the physics laboratory there he had found the draft of a note written by Röntgen to a manufacturer in which Röntgen stated that in case he could not buy tubes for the equivalent of five dollars each he would make them himself!

The relationship between the development of apparatus and the development of roentgenology in medicine is akin to the fundamental one that exists universally between structure and function. With the assumptions that apparatus has improved constantly since 1895; that improved apparatus has permitted better roentgenograms, and that better roentgenograms have brought different values and viewpoints into medicine, we shall henceforth, in attempting to trace the development of the roentgenologic examination of the gall bladder, confine ourselves to the medical concepts that have arisen, ignoring the improvements in armamentarium that have made them possible.

Although gallstones—the most conspicuous manifestation of gall-bladder pathology—apparently did not achieve description in medical literature until the fourteenth century (5), they have been found in an Egyptian mummy (6), and it does not seem unreasonable to suppose that disease of the biliary tract is as old as man himself. The present attitude toward gall-bladder disease, however, is in large measure derived from, and dominated by, surgery; and surgery of the gall bladder is but little older than the roentgen ray. The first operation on the gall bladder, in the existing sense of that term, was performed by Bobbs of Indianapolis (7), in 1867; and the procedures of biliary surgery were established in the twenty-odd years following, largely through the efforts of Sims, Tait, Langenbuch, Winiwarter and McBurney. In the first comprehensive article on this subject to appear in American literature, that of Musser and Keen (8) in 1884, the authors were able to find but thirty-five cases recorded in which "abdominal section was systematically performed." Musser observed that the most striking feature about these tabulated cases was "the wonderfully successful results of operative interference," in spite of the fact that there were ten post-operative deaths among the thirty-five. Previous to this evolution in surgery, it seems to have been the practice to treat by operation only those advanced cases with abscess formation in which the abscess pointed anteriorly, and then by aspiration or mere incision of the abdominal wall. And, probably because the therapy was so meager, the diagnosis in the less advanced cases received apparently but scant attention.

It was natural then, in the latter eighteen nineties, that physicians should seek to effect a liaison between the youthful clinical entity of gall-bladder disease and the newly discovered roentgen ray. In the discussion following Williams' paper (9) on the X-rays in medicine, presented before the Association of American Physicians on April 30, 1896, the only reference to their diagnostic use was a question from Osler, as to "whether the fluoroscope can detect gallstones." J. William White (10), in his paper before the American Surgical Association a year later, stated that "below the diaphragm the most interesting unsettled points relate to the value of the roentgen

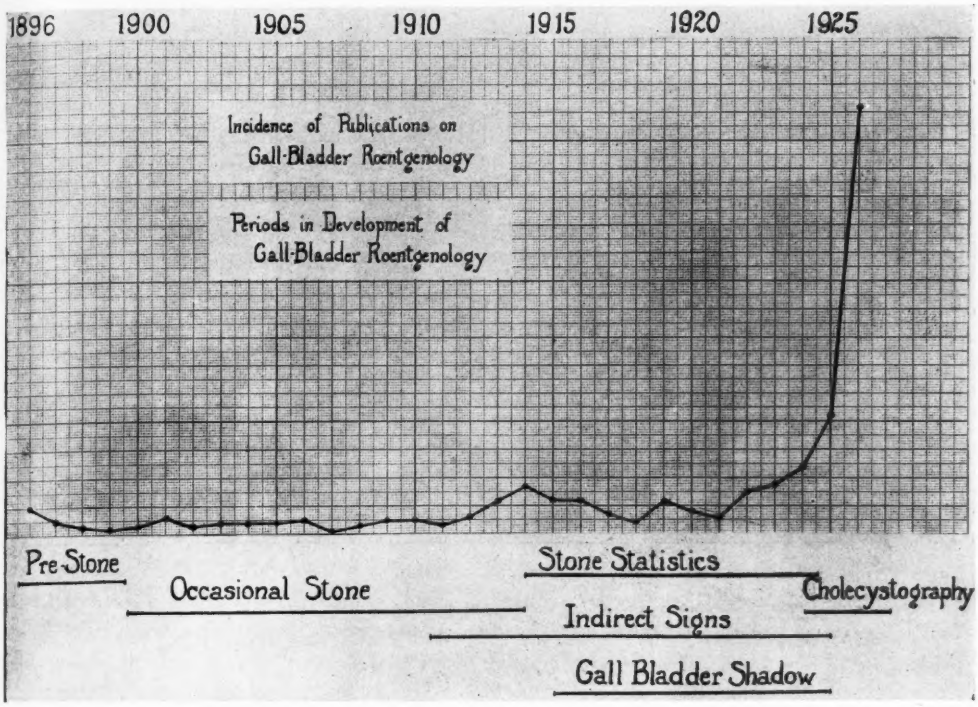

Fig. 1. Curve indicating number of articles pertaining to roentgenology of the gall bladder according to the year of publication, from 1896 to 1926, inclusive.
Approximate duration of the arbitrary periods of gall-bladder roentgenology indicated below.

ray in determining with certainty the presence or absence of various forms of calculi."

In essaying to outline the history of gall-bladder roentgenology we have relied entirely upon the record in the literature and have consulted most of the references bearing upon this subject of which we could obtain knowledge and which were accessible to us. These references were arranged chronologically and a curve plotted to show the relative number of contributions by years from 1896 to 1926. We regard this graph (Fig. 1) as representing the approximate degree of interest that has existed from time to time in the roentgenologic study of the gall bladder; and as indicating, after the initial period of experiment, the extent of employment and the clinical value of this study. The striking thing in this curve is the great height attained during the years 1925 and 1926, particularly in the latter.

The references were then considered according to their content and it was found that they dealt with a comparatively small group of concepts which seemed to have fairly definite time relations. That is, certain phases of subject matter appeared to dominate certain periods of time, although in no exclusive manner, as numerous articles referred to more than one concept, and therefore the duration of the various concepts to some extent overlapped. However, on the combined basis of time and subject it seems possible to divide the history of gall-bladder roentgenology into periods, and our attempt to do this results as follows:

1. Pre-stone Period, extending from 1895 to 1899.

2. Occasional Stone Period, from 1899 to 1913.

3. Period of Stone Statistics, from 1913 to 1924.

4. Period of Indirect Signs, from 1911 to 1925.

5. The Gall-bladder Shadow Era, from 1915 to 1925.

6. The Age of Cholecystography, from 1924 to present.

The approximate time extent of these various periods is marked below the curve showing the incidence of publications (Chart 1).

The Pre-stone Period should be regarded chiefly as an unsuccessful four-year quest for the radiographic demonstration of gallstones in the living. But although thwarted in its chief endeavor, it furnished several important observations. Thus it was shown that isolated gallstones could be visualized on the roentgen plate; that they might be demonstrated when placed in a cadaver; that they were probably less dense than renal calculi, and that they were of about the same density as the liver. It was the general conclusion that with the armamentarium then available they were impossible of demonstration in the living.

Insofar as I can ascertain, the first roentgenogram of an isolated gallstone to be published appeared in an article by Cattell (11), of Philadelphia, in the *Medical News* of February 15, 1896. Cattell placed a penny, a lead pencil, and a gallstone in a piece of small intestine containing mucus and fecal material and the whole was then radiographed with the assistance of Goodspeed, of the Physics Department of the University of Pennsylvania. In the copy of this journal which I have seen the calculus is identified with some difficulty, and a similar comment on the reproduction was made by Beck, in 1899. It is perhaps of incidental interest that Cattell should say that the entire cost of an X-ray apparatus need not exceed fifty dollars, and that this amount would shortly be materially diminished.

A contribution of interest in this period was that of White (10), in 1897, which, according to his acknowledgment, was based on technical work done by Leonard. He stated that in three cases calculi were "seen during the process of development of the plate, and were subsequently found and removed by operation, but no print showing their shadow was obtainable."

The first presentation of calculi in the living is credited to Carl Beck (12), a New York surgeon, who established this claim with the "skiagraphs" of two cases presented before the New York County Medical Association on October 16, 1899. The achievement of Beck, in accomplishing what was then generally regarded as impossible, was apparently not a circumstance of fortune but the fruition of diligence, for he states that he had been trying "experiments in this direction since February, 1896, by making ninety-seven skiagraphs in twenty-eight cases of suspected cholelithiasis," but, although the presence of calculi was revealed in nineteen of these by subsequent cholecystotomy, he had been unable to obtain any shadow of diagnostic value. In his first successful trial he employed four different photographic plates at the same time, one superimposed upon another. He states that "the upper plate, situated directly below the region of the gall bladder, showed well the outlines of the liver, while in the fourth and remotest it appeared only faintly, but the calculi were clearly represented." Later he demonstrated these same calculi with the use of a single plate. In the communication cited Beck emphasized three points in technic: first, the use of a proper tube and correct exposure time; second, the approximation of the gall bladder to the plate by elevating the clavicles and symphysis and by turning the body slightly to the right and raising the left side, and third, the direc-

tion of the rays from the side so as to avoid penetrating the whole diameter of the liver. In the years following this, Beck contributed several articles relative to the representation of calculi. In 1901 he stated that he had shown stones of pin-head size and those composed of pure cholesterin (13); and in 1906 he wrote that he had "found that a bladder containing stones and being fairly well filled with bile leaves a tumor-like shadow on the plate" (14).

His reports naturally stimulated others to try to duplicate and verify his results, but most of those who endeavored to do so were unsuccessful. Two years after his first announcement of success he stated that some had sustained his views but that others had assumed that his "skiagraphic interpretations were, to say the least, erroneous." And it must be admitted, I think, that the evidence in support of his interpretation of the two cases first reported is not altogether conclusive. There is no record that I can find of either case ever being jaundiced nor of having been operated upon; certainly such information is lacking in the initial report. In 1901 he stated that re-examination of the first case had failed to reveal the calculi and he assumed that they had passed away; and in 1906 he stated that this patient had passed two stones. Whether Beck was correct in his interpretation in these cases is of small moment in comparison with his manifold services to the roentgenologic examination of the gall bladder. His contribution to the study of isolated gallstones; his insistence upon proper technic in the examination of the patient (such as his position, which was widely quoted); his description of the gall-bladder shadow itself; his emphasis upon careful study of the plates, as by oblique illumination, and his numerous articles concerning the possibility of demonstrating stones in a certain number of cases kept the subject alive during a rather barren period, anticipated much that later authors emphasized, and merit his designation as the founder of gall-bladder roentgenology.

The Period of the Occasional Stone began with Beck in 1899 and continued until 1913. It is marked by its long extent without encroachment by other periods and by the comparative paucity of its contributions. Besides Beck's work, there were, from time to time, other reports of the demonstration of calculi, largely as incidental findings. These have been recorded in such comprehensive reviews as those of O'Brien (15), Knox (16), Haenisch (17), and Brailsford (18). There were also occasional references to the lack of clinical value of roentgenologic examination of the gall bladder. The culmination of the period was probably reached in 1910 when Pfahler, Haenisch, and Cole each reported the finding of stones in three cases. The general viewpoint during this period seems to have been that while gallstones might occasionally be shown on roentgen plates, the rarity of this occurrence made useless any systematic search for them.

Case (19), of Battle Creek, was the first to report the demonstration of gallstones in a considerable number of individuals and to refer the possibility of such demonstration to a percentage basis. In 1913 he announced that he had found calculi in 40 of 1,000 routine gastro-intestinal examinations and in 8 others, a number greater than the total of those hitherto recorded in the literature. Assuming, largely on the basis of autopsy statistics, that 10 per cent represented a generous estimate of the incidence of calculi in the living, and knowing that he had found them in 4 per cent of the gastro-intestinal and 4.8 per cent of the entire group considered, he concluded that gallstones could probably be shown in 40 or 50 per cent of all cases in which they were present. This publication of Case inaugurated what we have designated as the Period of Stone Statistics,—a period marked by the emphasis upon careful technic and studious interpre-

tation; the more detailed consideration of the various types of calculi; the introduction of attention to the differential diagnosis from other abdominal shadows; the presentation of the idea that failure to visualize stones might indicate their absence, and the revival of the belief first advocated by Beck, that the roentgenological search for calculi was a worth-while clinical procedure. All these manifestations developed, in large measure, from the fundamental observation that biliary calculi might be found in an appreciable percentage of the persons submitted to roentgenologic examination of the abdomen. Withal, this was a period of controversy, with varying opinions relative to the degree of perfection that might be attained in the demonstration and recognition of gallstones and the value of the quest for them.

Soon after Case's basic contribution, Cole (20) announced the finding of gallstones in 20 of 200 cases having gastro-intestinal examination, and Pfahler (21) reported having demonstrated them in 20 of 27 cases in which they were subsequently found at operation. Whereas Case and Cole seem to have first noted them more or less incidentally during the course of bismuth meal studies, Pfahler had made a particular examination of the gall-bladder region and had described a new and special position for the patient.

Subsequent reports relative to the possibilities of stone demonstration were fairly numerous and the estimates given varied from the statement of Cole and George (22), in 1915, that "it would now appear that we can show them in all cases where they are present" to the comparatively modest figure of 10 per cent given by Crane (23) in 1919 and by Bevan (24) in 1922. It was natural that attempts should be made to understand the reasons for this wide divergence in opinion. Knox (16) explained it, I think justly, as due largely to differences in technic and to the varying importance that was attached to doubtful shadows. These were the points most emphasized by those advocating the greater possibilities, who, although differing in the technical minutiæ described, were united in affirming that meticulous care in the execution of the examination and painstaking study of the resultant plates were essential to success.

Technic was admittedly important, but it could be fairly well standardized, and it seemed incredible that differences in technical procedure alone could account for any major portion of the wide discrepancy in the views presented. Apparently the greater basis for this conflict of opinion lay in the evaluation of shadows.

Various roentgenologic studies of isolated gallstones had indicated that the degree of their visibility was largely proportional to their mineral content, which was predominantly calcium, of which the great majority of stones contained but little, if any. George and Gerber (25) in 1914 spoke of two classes of calculi—"those that are easy to find and those that are difficult to see." The former group, containing a relatively large amount of calcium, could, according to Pfahler (26), "be shown by any technic and seen by anybody." This was the type of stone chiefly reported during the Period of the Occasional Stone and was the one whose presence now could not be denied, although its nature might sometimes be disputed. The doubtful shadows mentioned by Knox (16) occurred in the second group—those containing little or no calcium. The workers claiming the greatest success in the recognition of these referred to the special skill that was necessary in interpretation and proposed the employment of various aids to vision—magnification, oblique illumination, superimposition of plates, and the study of numerous plates in a single case. A few workers reported the demonstration of pure cholesterin stones as shadows of diminished

density, but mostly shadows of increased density of varying degrees of distinctness were described.

While certain roentgenologists were skeptical of the advances reported in the conquest of the essentially cholesterin calculi, it is probable that internists and surgeons were as a class more dubious. Stewart (27) remarked that "it is frequently impossible to demonstrate the presence of gallstones to the satisfaction of the attendant physician or surgeon"; and O'Brien (15) referred to "the type of stone that consultants question because they cannot detect it on the plate." Probably the keenest criticism against the profession of very great skill in the diagnosis of stones of low mineral content was made by Caldwell (28) in 1915. He pointed out that the refinements in examination which increased the chances of seeing the shadows of gallstones likewise accentuated the variations in density which might simulate these stone shadows. He asserted that "if only we make enough plates and make them well enough, we can obtain suspicious shadows in the gall-bladder region of any normal individual. The interpretation of gallstone plates, therefore, becomes a matter involving not only skill and judgment, but temperament as well. In no other field of roentgen diagnosis is the personal equation of the observer more important." He also remarked that calculi are so common in cases submitted to gall-bladder operation that a positive diagnosis made on the basis of suspicious shadows was not of necessity sound, merely because stones were revealed by the surgical intervention.

With the increasing number of gallstones found, their differential diagnosis from simulating shadows of other origin—such as renal calculi, calcified mesenteric glands, and calcified costal cartilages—became of importance. Considerable was written relative to the aids in this differentiation—stereoscopy, lateral views, comparison of antero-posterior with postero-anterior views and the character of the shadows themselves were some of these aids mentioned most frequently. This increase in demonstrability also occasioned some to regard the failure to find stone shadows as more or less indicative of their absence, but the value of a negative finding was never much emphasized.

The Period of Stone Statistics may be said to have extended from 1913 until 1924, with its greatest development in the earlier of these years. The differences of opinion as to the demonstrability of stones remained matters of opinion. The figure probably most generally accepted in this country was that given by Carman and his associates (29), in 1924, of 38.4 per cent of calculi shown roentgenologically in 226 cases in which they were found at operation.

In the course of an address before the American Roentgen Ray Society in 1916, C. H. Mayo (30) stated that "undoubtedly a great deal of effort has been wasted by the roentgenologist in endeavoring to diagnose gallstones." He explained this statement by adding that even if the diagnosis of stones could be 100 per cent correct, the method would still avail nothing in the large group of patients having other than calculous disease of the gall bladder.

Roentgenologists had already, however, presented arguments to show that they might detect other manifestations of biliary pathology than the presence of stones. The evidence offered by them was obtained during the examination of the gastro-intestinal tract by means of a radiopaque substance—a method of examination anticipated by many, but only generally established and respected since the work of Rieder (31, 32) in 1904. Probably the first publication referring directly to the value of information obtained in this way was that of Pfahler (33), of Philadelphia, appearing in 1911 and entitled "Gastric and Duodenal Ad-

hesions in the Gall-bladder Region, and Their Diagnosis by the Roentgen Rays." It stated that in chronic gall-bladder disease, swelling of the liver and gall bladder brought them closer to the duodenum and stomach; pericystitis led to adhesions; then, when the swelling became reduced, the adhesions pulled the stomach and duodenum upward and to the right. This change in the position of these organs, which could be best recognized fluoroscopically, permitted the diagnosis of cholecystitis to be made. In the presence of adhesions about the gall bladder, this method of examination, according to Pfahler, was distinctly more valuable than the direct search for stones.

The nature and worth of the data to be obtained from these gastro-intestinal studies were elaborated upon by Case (19) in 1913, Cole (20) in 1914, and by numerous others in the years that followed. The evidence itself came to be generally designated as "indirect," or, more rarely, "secondary," in contradistinction to the shadows of calculi or of the gall bladder itself, which were called "direct." This differentiation in terminology was employed first, I believe, by Cole.

The number of signs described whereby gall-bladder lesions might be inferred from observations made on the form and behavior of the main gastro-intestinal lumen were legion. They fall mostly, however, into three well defined groups in accordance with the explanations given as to the manner of their origin. First, there were pressure effects, evident as impressions in the outline of duodenum, stomach, and occasionally colon, and due supposedly to the weight of a diseased gall bladder. Second, there were traction effects, manifest in the abnormal position or deformity of the stomach, duodenum, or colon, and caused presumably by adhesions incident upon a pericholecystitis. Third, there were various so-called reflex effects consisting of alterations in behavior instead of distortions in anatomy. These reflex effects, such as spasm of the stomach or duodenum, cardiac regurgitation, and gastric hypermotility, were, however, rarely ever regarded as specific for biliary disease. And finally, a few signs were presented which do not seem to belong properly in any of the above classes; among these were retention of barium in the ampulla of Vater, and a small area of tenderness localized to the outer side of the duodenum.

The more zealous advocates of these indirect signs regarded their presence as being of more consequence in the evaluation of gall-bladder disease than the positive demonstration of stones. This belief was based on the assumption that stones might exist without any significant pathologic change in the gall bladder itself, whereas indirect signs could occur only in association with a definite cholecystitis. On the other hand, there were workers of distinction who placed no credence in either the demonstration or interpretation of these indirect signs.

The sign advocated most forcefully and regarded as most common in occurrence was the pressure defect on the duodenum or antrum, which was presented by its chief proponents as having a quite characteristic appearance and being almost pathognomonic of a diseased gall bladder. It was generally accepted that most of these crescentic impressions were due to the gall bladder, but it was not generally held that a gall bladder need be pathologic in order to produce such an impression. Case (34), in 1926, showed that in so far as cholecystography could be invoked in judgment, a normal gall bladder might produce a classical indentation. Disturbances from adhesions were also emphasized, and, while admittedly adhesions from a pericholecystitis might occasion deformity and transposition of the neighboring viscera, it could not be denied that congenital bands and adhesions resulting from a localized peritonitis arising outside the gall bladder might cause similar appearances.

Besides the indirect signs, gastro-intestinal examination with the contrast meal was considered by some to supply information of another sort relative to gall-bladder diagnosis—the so-called "eliminative evidence." Skinner (35) referred to this as follows: "In many of these gastro-intestinal cases, if a patient has stomach symptoms severe enough to have prompted the internist to refer the case for a roentgen examination, there is trouble somewhere. If the roentgen examination determines a normal stomach and duodenum, a non-visualized appendix and no pain in the appendix region by palpation under the fluoroscope, there is a 90 per cent chance that gall-bladder disease is present."

The Period of Indirect Signs, which began with Pfahler's report in 1911, has existed until the present, although in quite attenuated form since the advent of cholecystography. While probably most physicians have agreed that a roentgenologic examination of the gastro-intestinal tract is of value in numerous patients suspected of cholecystitis, the meaning and importance of the indirect signs have remained matters of divergent opinions.

In 1904, Carl Beck (36) wrote that "the outlines of the gall bladder are often shown if there is cholelithiasis. On account of the long-continued irritation, the bladder walls become thick and fibrous and consequently less permeable to the rays." Although there were occasional references such as this to the roentgenologic visualization of the gall bladder, the subject attained no importance until 1915, when George, of Boston (37), announced "that when one can demonstrate a gall bladder it is pathological." In the next year this idea was elaborated upon by George and Leonard (38) together, their argument being somewhat as follows: As the result of previous observations, they had assumed that whenever a gall bladder is visualized it is pathologic. This hypothesis had been applied in the interpretation of plates, and the high incidence of operative verification of their interpretations had convinced them that their assumption was "a safe and reliable diagnostic aid."

The belief that every roentgenologically visualized gall bladder is diseased obtained a wide acceptance among clinicians as well as roentgenologists, both in this country and abroad. It was not universally accepted, however, and certain weighty criticisms were directed against the validity and value of the concept. In the first place, its field of utility was obviously limited, since its adherents admitted that probably the majority of diseased gall bladders did not produce definite shadows. In the second place, it was difficult to apply, since it was generally conceded that the recognition of the gall-bladder shadow was not easy. Although much was written relative to the manner of differentiating this shadow from the simulating shadows that originated in the abdomen, there were always some who believed that the uncertainty in this differentiation rendered the concept worthless. Carman and his associates (29) stated that shadows typical of the gall bladder might be seen in the roentgenograms of patients from whom the gall bladder had been removed; and Case (34), in 1926, said that in cholecystograms, shadows capable of representing the gall bladder had been observed apart from the shadow of the dye-filled viscus itself. And finally the truth of the postulate was questioned. Cases were cited in which a gall-bladder shadow was seen on the roentgenogram and a normal gall bladder found at operation. The advocates of the concept met this reproach by appealing from the decision of the surgeon—based upon inspection and palpation at operation —to the higher court of the pathologist, and affirmed that no gall bladder should be considered normal until after it had been submitted to a careful microscopic exam-

ination. This appeal was made as early as 1916 and is of interest as being a forewarning that sometime it might be advisable to try to define a pathologic gall bladder before laboring too much toward its recognition.

In 1924 the comprehensive study of Carman, MacCarty and Camp (29) presented the testimony of the pathologist relative to gall-bladder disease more forcefully than it had hitherto appeared in roentgenologic literature. MacCarty had found but 17 normal gall bladders in a series of 5,000 removed at operation. This indicated, in their opinion, that practically every adult gall bladder is diseased. "Consequently," they said, "assured before an examination of the support of the pathologist and usually of the surgeon, the roentgenologist needs only to discover a sign consistent with the presence of cholecystitis, and his percentage of correct diagnoses will be exceptionally high." Their analysis of a large group of cases indicated that a severely diseased gall bladder was no more likely to produce a shadow on the roentgenogram than one with but slight pathologic changes.

The Periods of Stone Statistics, Indirect Signs, and Gall-bladder Shadows had their origins, attained their greatest development, and met their severest criticisms within the United States. Although, with the exception of the one of George and Leonard (39), this country produced no such monographic studies of gall-bladder roentgenology as those of Knox (16), Haenisch (17), Duval, Gatellier and Béclère (40), and others, foreign literature, insofar as I can find, offers little in the way of viewpoints on this subject which had not been anticipated in this country.

One can only surmise as to how widely the doctrines of these periods were accepted and applied. In the hope of ascertaining some information relative to this in the case of a single institution, we have computed the number of roentgenologic examinations of the gastro-intestinal tract proper with the opaque meal, and of the gall-bladder region alone, made in Lakeside Hospital for each year between 1911 and 1926, and compared their variations with that of the total number of roentgenologic examinations made during this period, as shown in Chart 2. The striking thing displayed by this graph is the great increase in the number of gall-bladder examinations made during the last two years. It is our impression that in 1924 —twenty-five years after the first accepted demonstration of gallstones in the living by the roentgen ray—the majority of physicians believed that the occasional demonstration of calculi was the only direct service to be rendered by roentgenology toward the diagnosis of cholecystic disease.

In 1871, shortly after Bobbs performed the first gall-bladder operation, a German chemist named von Bayer (41) discovered a group of compounds called the phthaleins. In 1901, near the close of the Occasional Stone Period, experiments in a laboratory of pharmacology indicated that, when injected into the body, certain of these phthaleins were excreted chiefly through the liver, and others largely by way of the kidney. This pharmacologic study was made by Abel and Rowntree (42) in the hope of finding a serviceable hypodermic purgative. In the achievement of this, their chief aim, they were not particularly successful, but from the by-products of their work there were developed a test of kidney function, that has rendered abundant service (43), a test of liver function, which is probably more satisfactory than any other (44), and finally, through the labors of Graham and Cole, of St. Louis (45), a test of gall-bladder function, which has revolutionized gall-bladder roentgenology.

Graham and Cole's first communication appeared in February, 1924. In it they stated that, realizing the value of the con-

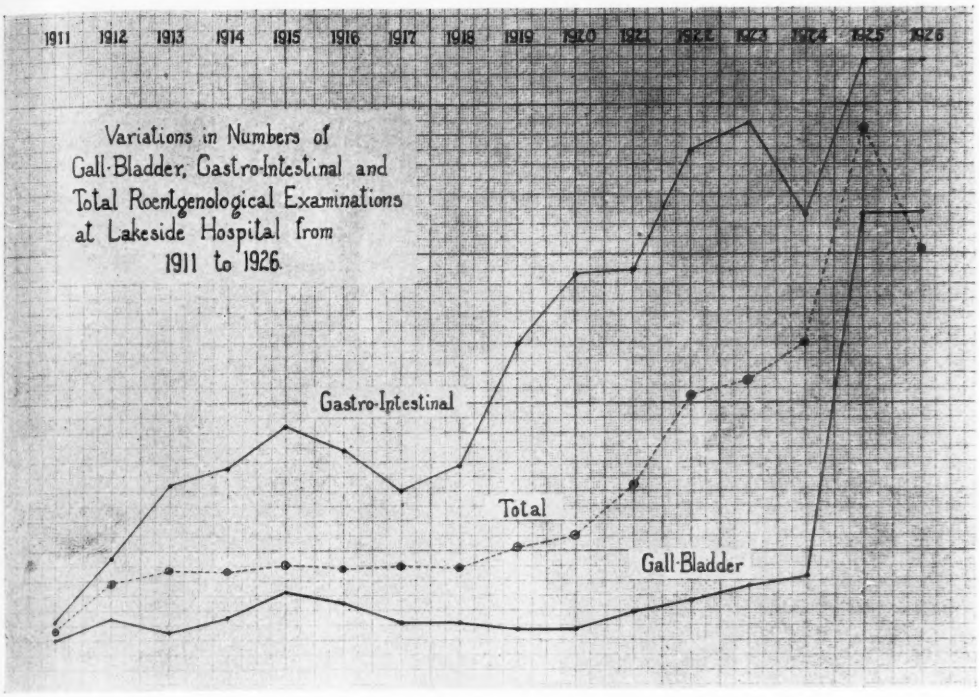
1911 1912 1913 1914 1915 1916 1917 1918 1919 1920 1921 1922 1923 1924 1925 1926
Variations in Numbers of Gall-Bladder, Gastro-Intestinal and Total Roentgenological Examinations at Lakeside Hospital from 1911 to 1926.
Gastro-Intestinal
Total
Gall-Bladder

Fig. 2. Curve showing the number of patients referred for opaque meal examinations of the gastro-intestinal tract and the number referred for examinations of the gall-bladder region alone, at Lakeside Hospital, Cleveland, during the years 1911 to 1926, inclusive. The variation in the total number of roentgenologic examinations is shown by the broken line.

trast meal in gastro-intestinal diagnosis, they had sought to depict the gall bladder in a similar manner by finding an opaque substance which, when introduced into the body, would be excreted into the bile; and which, when used in the concentrations necessary for the shadow of the gall bladder to be seen, would be devoid of toxic effects. They announced that the calcium salt of tetrabromphenolphthalein met these requirements both in experimental animals and in human beings.

With this announcement the Age of Cholecystography began. Before considering it, however, we should like to mention two contributions which preceded its advent and which may have been prophetic of its coming. The first was that of McNeil (46), in 1916, who modified the phenoltetrachlorphthalein test of liver function by collecting duodenal contents through a duodenal tube at intervals after the intravenous injection of the salt and analyzing the specimens thus obtained for their content of the injected substance. The second was that of Burckhardt and Müller (47), in 1920, who elaborated upon Whittaker's (48) method of detecting gallstones with the exploring needle, by introducing a cannula through the liver into the gall bladder of the living patient, injecting collargol or air into the viscus, and then radiographing it. By this method they secured roentgenograms of biliary calculi quite similar to those that are now obtained with cholecystography.

The Age of Cholecystography developed slowly for a time, but within little more than a year after its birth it was—I believe

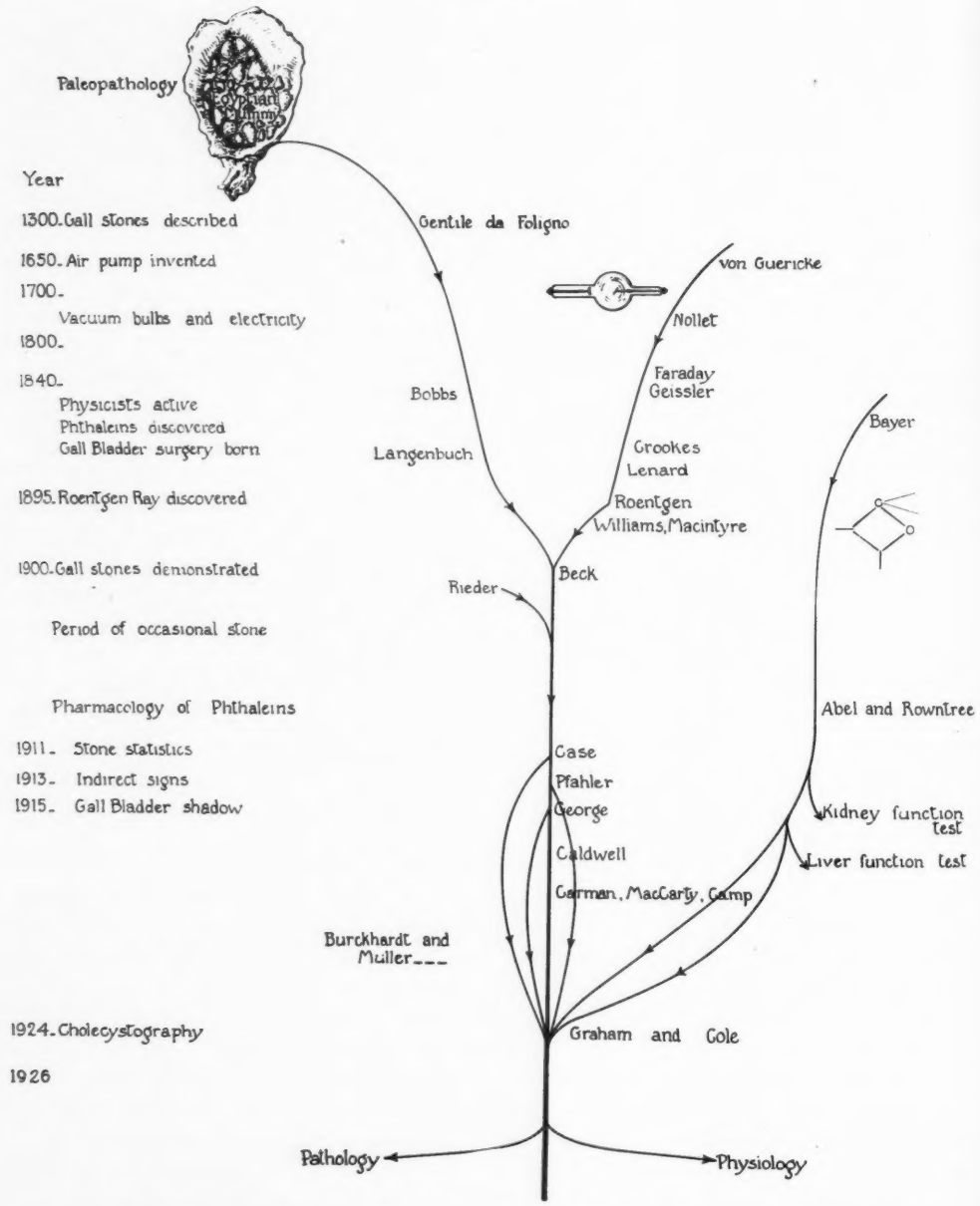

Fig. 3. Schematic representation of the history of the gall bladder, the arrows indicating the direction in which knowledge has passed.

we may say—the dominant interest in roentgenology throughout the world. The marked increase in contributions to the literature for the years 1925 and 1926, as shown in Chart 1, attest to the great extent of this interest. With the maturing of cholecystography in 1925 we may consider the Period of Indirect Signs and that of the

Gall-bladder Shadow as practically coming to an end, or, at least, becoming quiescent. For, although in the literature of this country at least, they have probably been upheld almost as often since then as before, the attention devoted to them has still been insignificant in comparison to that given to cholecystography.

The developments that have thus far occurred in cholecystography are so recent and so well known that any attempt on our part to outline them might well merit the contempt that is often afforded familiarity. Hence we shall present cholecystography only as the existing culmination of the roentgenologic study of the gall bladder—a method of study which has obtained wide acclaim as an aid in clinical diagnosis, contributed to a broader knowledge of biliary pathology, and assisted toward the better understanding of gall-bladder physiology.

Figure 3 is an attempt to portray pictorially the main currents of knowledge in the development of the roentgenology of the gall bladder—a story that began in the pure springs of physics, flowed through the marches of controversy around Stone Statistics, Indirect Signs, and Gall-bladder Shadows, and emerged in the broad stream of Cholecystography, which has overflowed the banks of clinical medicine to irrigate the fields of pathology and physiology.

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CORRELATION OF CHOLECYSTOGRAPHY AND THE BARIUM MEAL[1]

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CHOLECYSTOGRAPHY has now been long enough in use so that we are getting a fair idea of its value. At first we thought its most reliable feature was the dye-filled gall bladder, signifying absence of pathology, while a faint or absent shadow, indicating disease, was less reliable. This was especially true of the oral method. Now, however, with proper administration of the dye, and assurance of its assimilation, we place great reliance on faint or absent shadow as pointing to pathology, while a positive shadow does not necessarily mean a healthy gall bladder. In fact, approximately 25 per cent of dye-filled gall bladders may harbor pathology, which will be missed by the roentgenologist unless other measures of diagnosis are used.

In an effort to reduce this percentage of error I have analyzed over 300 consecutive cases in which both cholecystography and the barium meal examination have been done in my office and hospital practice. Of these cases, 75 were done by my predecessor, Dr. B. R. Kirklin, and 230 by myself. Tabulations of these cases set forth the principal data. The routine, with few exceptions, has been as follows: The patient is given capsules containing 5 grains each of sodium tetraiodophenolphthalein, one capsule for each 15 pounds of body-weight, but not to exceed 15 capsules in any case, and not less than 8 capsules to an adult. These capsules are taken in five doses, as nearly equal as possible, the first just before the evening meal, the second during the meal, the third immediately after the meal, and the other two at intervals of a half-hour after the meal. Instructions are given for the evening meal to be free from meat, eggs, or milk; to follow the third dose of capsules with a half-teaspoonful of soda, and to drink freely of fluid during the evening. The patient reports for examination the following morning at nine or ten o'clock, without breakfast. Careful questioning elicits data as to nausea, vomiting, or diarrhea, and these are recorded. The first gall-bladder exposure is made on a film large enough to include the cecum, so as to register undissolved dye, and to catch an abnormally low gall bladder. If no dye shadow is registered, further exposures are at once made on smaller films, with varying technic. If the patient has admitted vomiting within one and a half hours after the last capsules were taken, and if no dye shadow or a faint shadow is found on the films, the test is usually repeated a few days later. I have had only one case in which there was vomiting the second time, and that was pernicious vomiting of pregnancy. If the patient gives a story of diarrhea beginning within a few hours after the last dose of capsules, and if the films show a faint shadow or none at all, the test is also repeated later. As soon as the first gall-bladder films are inspected, the barium meal is at once given, according to the usual technic. Serial films are taken, and these often give important information as to the relation of the gall bladder to the stomach and duodenum. At noon another gall-bladder film is made; if the morning film has registered a good dye shadow, the noon film usually also shows a good shadow, with additional information as to relations of gall bladder to the hollow viscera. The patient is then instructed to eat a light meal at two o'clock, with a generous amount of fat,

[1]Presented before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

usually cream or butter; then at four o'clock another fluoroscopic observation is made, and final gall-bladder films show its emptying power. Persistent barium deposits are sometimes seen in peptic ulcer craters, duodenal diverticula, ampullæ of Vater, or fistulous tracts between gall bladder and intestine. Subsequent observations of the barium meal are usually made the following day, and occasionally a persistent gall-bladder shadow is noted. It is extremely seldom that the barium-meal shadows interfere with the visualization of the gall bladder. The ingestion of food at 2 P. M. has never to my knowledge in this series given rise to any misinterpretation at the six-hour observation of the barium meal.

Table I gives a résumé of the principal data of 305 consecutive cases receiving both the gall-bladder dye and the barium meal. The number of cases diagnosed as gall-bladder pathology (162) is greater than all the other cases combined. This may seem excessive and excite doubt as to the validity of the diagnoses. A later table, however, will show that, of the cases coming to absolute proof, 97.3 per cent corroborated the X-ray findings.

TABLE I

Total number in series		305
A.	Number of men	140
B.	Number of women	165
C.	Average age men	45½ Yrs.
D.	Average age women	42 Yrs.
E.	Average age of total	43 Yrs.
F.	X-ray diagnosis pathologic gall bladder	162
G.	Men	66
H.	Women	96
J.	X-ray diagnosis indeterminate	6
K.	X-ray diagnosis no pathology found	68
L.	Men	30
M.	Women	38
N.	X-ray diagnosis other pathology than gall bladder	69
P.	Duodenal ulcer, alone and complicated	31
R.	Appendicitis, alone and complicated	22
S.	Gastric ulcer, alone and complicated	3

Table II shows the incidence of diagnostic data based on cholecystography and the barium meal. In no instance was gall-bladder disease reported on "indirect" evidence alone (Item B), but its possibility must be admitted. More than one-third (57) of the cases reported as gall-bladder pathology showed no "indirect" evidence of it, or no evidence was recorded (Item C), the diagnosis depending on the cholecystogram alone. The term "indirect evidence" refers to the abnormalities of behavior, outline, and position of the several parts of the gastro-intestinal tract that are known to occur in gall-bladder disease. This phase of diagnosis used to receive much attention from such men as George, Cole, Case, Pfahler, Kirklin, and others, but has been overshadowed by the striking success of cholecystography as devised by Graham and his associates, and signally developed by Menees, Whitaker, etc. Of course, it must be realized that many of the "indirect signs" are just as truly signs of other pathology, and are in no sense limited to gall-bladder disease. Items B and D in Table II indicate this very plainly. The present series points toward adhesions and pressure deformities as being the most significant "indirect" signs of gall-bladder disease, confirming the analysis of a previous series.[2] However, they may sometimes occur in other conditions, and therefore are not pathognomonic.

TABLE II

A.	Cases showing both dye evidence and indirect evidence of pathologic gall bladder	105
B.	Cases showing indirect evidence but no dye evidence of pathologic gall bladder	36
C.	Cases showing dye evidence but no indirect evidence of pathologic gall bladder	57
D.	Cases showing indirect evidence, but no dye evidence, and diagnosis made of pathology other than gall bladder	22

In Table III, Item B shows that gallstones were detected in only 13.6 per cent of the cases reported as gall-bladder disease. The

2RADIOLOGY, September, 1926, VII, 201.

usual incidence of calculi is much greater, as shown by statistics. Deaver found calculi in 50 per cent of a series of over 900 cases operated upon, though it must be borne in mind that gallstone cases come much quicker to surgery than non-calculous cases. Diagnosis of cholecystic disease was made more often on faint shadow (Item H) than on absent shadow (Item G), and this was also true of the cases operated upon (Table XI, Items A and D). Item L shows 15 cases reported as calculi, due to negative shadows against a background of dye shadow. These calculi would probably never have been detected by old methods. Irregularities of shape and size (Item K) play little part in diagnosis. The phenomenon of delayed emptying was occasionally the basis for a diagnosis of pathology, but usually it was found in cases of stones or a shadow that was faint in the beginning.

TABLE III

A.	Cases diagnosed as pathologic gall bladder by X-ray	162
B.	Cases diagnosed as gallstones (all women)	22 = 13.6%
C.	Cases diagnosed as pathologic gall bladder and also other pathology	23
D.	Men	13
E.	Women	10
F.	Cases showing pathologic gall bladder and also duodenal ulcer	6
G.	Cases showing no dye shadow	65
H.	Cases showing subnormal shadow	72
J.	Cases showing delayed emptying	32
K.	Cases showing irregularities of shape or size	23
L.	Cases showing negative shadows of gallstones	15
M.	Cases showing positive shadows of gallstones	7

The occurrence of vomiting after oral administration of the dye was rather rare (Item C, Table IV). Frequently a good shadow developed, despite the vomiting, and always if the vomiting did not occur till one and a half hours after taking the last capsule. The test had to be repeated only 12 times, and only once was the second trial a failure—in a case of pernicious vomiting of pregnancy.

TABLE IV

Effects of the Dye

A.	Effects recorded in	228 cases	
B.	Nausea in	72 cases	31.6%
C.	Vomiting in	25 cases	10.9%
D.	Diarrhea in	29 cases	12.7%
E.	Dye repeated	12 cases	5.2%
F.	Because of vomiting	10	
G.	Because of diarrhea	2	

"Indirect" signs were observed in 105 out of 162 cases diagnosed as gall-bladder pathology. Table V analyzes these signs. Spastic antrum, often assuming a funnel or tubular shape, always directs attention to the likelihood of gall-bladder disease (Item B). A spastic pylorus denotes a resistance to peristaltic effort, with intermittent or delayed relaxation to allow passage of barium. Adhesive changes (Items D, E, F, G, H) were frequent, especially affecting the bulb, which was usually displaced downward to the right. The bulb was seen to be deformed in many instances where there was doubt whether it was due to adhesions or spasm (Item K). Regurgitation was recorded in 6 cases (Item S), the barium shooting back from the fourth, third, or second part into the bulb, but never into the stomach. Esophageal regurgitation was never observed.

TABLE V

Indirect Evidence was Observed in 105 of 162 Cases Diagnosed as Gall-bladder Pathology

A.	Spastic changes		65
B.	Stomach, usually antrum or pylorus	30	
C.	Duodenal, usually bulb	35	
D.	Adhesive changes		42
E.	Stomach, usually antrum or pylorus	6	
F.	Duodenum, bulb or second part	29	
G.	Colon, usually hepatic flexure	4	

H.	Jejunum	3
J.	Pressure deformities, stomach or duodenum	8
K.	Bulb deformities, unclassified	28
L.	Motility changes	50
M.	Hypermotility	18
N.	Hyperperistalsis	13
P.	Gastric fluid	7
R.	Gastric barium residue	6
S.	Duodenal regurgitation	6
T.	Ampulla of Vater dilated	2

Among the series of 143 cases showing no gall-bladder disease, there were 20 which showed a normal cholecystogram, and "indirect" evidence, with a diagnosis of pathology elsewhere than in the gall bladder. These are set forth in Table VI. It is noticeable that adhesive signs were recorded only once (Items E, F, G). It is quite apparent once more that the other "indirect" signs are common to disease located elsewhere than in the bile tract.

TABLE VII

Indirect Evidence, with Normal Dye Shadow, and Pathology Other Than Gall Bladder

A.	Pathologic appendix	10
B.	Dental pathology	4
C.	Enlarged heart	2
D.	Neurasthenia	1
E.	Colonic obstruction	1
F.	Cecal disease	1
G.	Tuberculosis of lungs	1

In the total series of 305, there were 68 reported as negative for any pathology by X-ray. Out of these 68 there were 36 that showed a normal cholecystogram and positive "indirect" signs, as analyzed in Table VIII. These signs once more are seen to comprise mostly the spastic deformities (Items A, B, C) and disorders of motility (Items J, K, L, M). Adhesions were recorded 4 times (Items E, F, G); there is no means of knowing whether these 4 cases actually had cholecystic disease or not, but

TABLE VI

Indirect Signs in 20 Cases Reported as Negative for Gall-bladder Pathology, but Positive for Other Disease

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
A. Gastric spasm		1																			1
B. Pylorospasm														1		1		1			3
C. Bulb spasm			1	1	1		1	1	1	1			1	1		1		1			11
D. Bulb deformity															1		1				2
E. Duodenal adhesions																				1	1
F. Colon adhesions																					0
G. Antral adhesions																					0
H. Pressure																					0
J. Hypermotility	1					1			1	1	1	1							1		7
K. Hyperperistalsis	1					1			1	1											4
L. Fluid in stomach												1									1
M. Duodenal regurgitation												1									1
	2	1	1	1	1	2	1	1	3	3	1	3	1	2	1	2	1	2	1	1	

The diagnoses reported in the cases in Table VI are shown in Table VII, where appendicitis is the most frequent disease. The variety of conditions is in keeping with previous reviewers, who have found spastic changes and altered motility in pathology of remote origin.

at least we know that gall-bladder adhesions are compatible with a normal cholecystogram. The evidence was not deemed sufficient to report a pathologic gall bladder or peptic ulcer. One case of pressure deformity with a normal gall-bladder shadow was observed (Item H), which raises again the

TABLE VIII

36 Cases Reported as Negative, with Normal Dye Shadow, but Positive Indirect Signs

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	
A. Gastric spasm								1																									1				2
B. Pylorospasm																			1			1									1			1		4
C. Bulb spasm	1	1		1	1	1	1			1	1			1	1	1				1		1		1			1				1	1	1			18
D. Bulb deformity		1						1	1									1	1				1											1	1	1	9
E. Duodenal adhesions																					1																1
F. Colon adhesions																							1														1
G. Antral adhesions			1								1																										2
H. Pressure						1																															1
J. Hypermotility	1												1						1		1		1		1				1	1							8
K. Hyperperistalsis	1									1		1	1	1	1				1				1		1	1	1		1	1							13
L. Fluid in stomach					1											1																					2
M. Duodenal regurgitation																	1						1		1			1	1								5
	3	2	1	1	2	2	1	2	1	2	2	1	2	2	2	2	1	1	4	1	2	2	5	1	3	1	2	1	3	2	2	1	2	1	2	1	

question whether a pressure deformity is pathognomonic of cholecystic disease.

Of 162 cases reported by X-ray, as gall-bladder pathology, there were 37 that came to ultimate proof by operation or necropsy, shown in Table IX. The percentage of corroboration was 97.3 per cent. The one case where the X-ray report of gall-bladder pathology was not confirmed was a cancer of the ascending colon; the cholecystogram had been very faint, but the surgeon, after inspection and palpation of the gall bladder, declared it normal. Gallstones were revealed in about half the cases (Item D). It is interesting to note that the X-ray discovery of stones was made in women only (Item E), but missed in all the men (Item F). X-ray examination predicted gallstones in 10 cases, 52.6 per cent, all proved correct (Item G). In six of these cases the stones were suggested by negative shadows or mottling of a more or less distinct dye shadow. It is safe to say that without the dye the calculi would have been missed in all these cases, which would have reduced the detected gallstone cases to 4, or 21.5 per cent. In the 9 cases of calculi that escaped detection by X-ray, there was no dye shadow in 5 and hence no chance to register the contrast mottling. Of the remaining 4 that were missed, 2 had unsatisfactory films, and one, on being reviewed, revealed a mottling that should have aroused suspicion. Of the 6 cases of gallstones in men, shown at operation, but missed by X-ray examination, 4 registered no dye filling, and one received poor technical work; 2 of the men were very large and heavy.

TABLE IX

Out of 162 Cases Diagnosed as Pathologic Gall Bladder, the Number Known to Come to Operation or Autopsy, with Records Available, Is 37

A.	Women	24	
B.	Men	13	
C.	Pathologic gall bladder was proved in 36 cases		97.3%
D.	Cases proved to have gallstones	19	51.4%
E.	Women	13	
F.	Men	6	
G.	Cases of gallstones diagnosed by X-ray	10	52.6%
H.	Women	10	
J.	Men	0	
K.	Cases showing indirect evidence	24 out of 37	64.8%
L.	Cases of proved gallstones showing indirect evidence	13 out of 19	68.4%
M.	Cholecystectomies		31
N.	Pathologist's report in		29
O.	Cholecystotomies		3
P.	Exploratory		2
R.	Necropsy		1

Twenty-four out of 37 cases (64.8 per cent) exhibited "indirect" signs (Item K);

of the 19 cases of calculi, 13 (68.4 per cent) exhibited "indirect" signs (Item L). Cholecystectomy was done in 31 cases (Item M), and 29 of the removed gall bladders were examined macroscopically by a pathologist.

Table X analyzes the 37 cases operated on with respect to the "indirect" signs they exhibited by X-ray examination. The most significant point is the frequency of adhesive signs (Item D); 12 out of 37, or 32.4 per cent. The operative records mentioned adhesions in 19 cases, or 51.4 per cent. Some of these adhesions were between the gall bladder and liver, or omentum, which are seldom possible to distinguish by X-ray examination, but other cases of adhesions probably should have been recorded.

TABLE XI

Gall-bladder Reaction to Dye in 36 Cases Wherein Operation Confirmed Diagnosis

A.	No dye shadow	14
B.	Proved to have stones	9
C.	Proved not to have stones	5
D.	Faint dye shadow	17
E.	Proved to have stones	9
F.	Proved not to have stones	8
G.	Distinct dye shadow	5
H.	1 persistent proved to have adhesions	
J.	1 persistent proved to have adhesions and thickening	
K.	1 persistent proved to be strawberry type	
L.	1 persistent proved to have adhesions, thin walls	
M.	1 enlarged shadow with constriction and stone	

CONCLUSIONS

The series of cases is too small to warrant definite conclusions of a sweeping

TABLE X

Indirect Evidence of Gall-bladder Disease in 37 Cases Submitted to Section

A. Cases showing indirect evidence	24
B. Cases showing none	6
C. Cases with no detailed records	7

D. Adhesions	1				1	1			1	1	1			1					1	1	1	1		1	12
E. Pressure												1			1			1							3
F. Spasm	1	1	1	1			1	1						1		1	1		1				1		11
G. Motor	1				1					1		1	1		1		1						1	1	9
H.	3	1	1	1	1	2	1	1	1	1	2	1	1	3	1	2	1	2	2	1	1	1	2	2	35

Table XI records the pathology found at operation as related to the character of the dye reaction. Stones occurred relatively oftener in gall bladders that showed no dye shadow (Item B), and this suggests that we still need to seek a method which will increase our ability to detect biliary calculi. If stones are present in a viscus that receives the dye, they are perceived in the great majority of cases. Five cases showed a distinct dye shadow (Item G), which was, however, persistent (delayed emptying) or deformed, or contained a calculus of lime density. Seven cases registered one or more stones with calcium content

nature. It strengthens our confidence in cholecystography, however, for 97.3 per cent of a series of cases operated upon confirmed the X-ray diagnosis, whereas in a series of 70 cases operated upon, previously reported, only 53 per cent were correctly diagnosed, using the old methods.

The darker side of the statistics would undoubtedly lie in the 143 cases where a normal cholecystographic response was observed, and no diagnosis of gall-bladder pathology was ventured. Some of these cases showed "indirect" signs, including adhesions. None of them has come to section, to my knowledge. Probably a certain pro-

portion of them are actually afflicted with gall-bladder disease, chiefly of the kind associated with adhesions or a strawberry type viscus. If a further study of "indirect" signs, in connection with cholecystography and surgery, should enable us to cut down the percentage of missed pathology, it would be worth while. We may derive a little comfort from the fact that operative treatment of these cases of mild pathology, with unimpaired function and a normal cholecystogram, is not so beneficial as in cases where function is deranged. The latter cases are usually detected by cholecystography.

Finally, I have found that "indirect" signs stimulate a more careful search for pathology, either in the gall bladder or elsewhere. They have also afforded sufficient confirmation in a few cases of absent or faint dye shadow, so that a repetition of the Graham test could be dispensed with. It seems quite certain that we cannot yet omit the barium meal in our efforts to detect gall-bladder pathology.

THE NORMAL CHOLECYSTOGRAPHIC RESPONSE[1]

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IN view of its remarkable achievements cholecystography cannot justly be the object of grave fault-finding. Most roentgenologists, myself among them, have shared heartily in the enthusiasm with which this diagnostic procedure has been greeted, and practical experience with it has, in the main, been highly satisfactory. It may be of service, however, to point out that the extensive literature of cholecystography is concerned almost wholly with the abnormal cholecystogram and its extraordinary value in the diagnosis of cholecystic disease. With certain reservations, which have received little stress, it has been assumed that a normal cholecystogram implies a normal gall bladder. Now this assumption, although valid in the majority of instances, must not be taken too implicitly, for, as I shall show, the normal cholecystogram is often responsible for error in diagnosis.

When the cholecystographic compound is given by mouth a normal response to the test indicates (1) satisfactory absorption of the drug into the circulation, (2) excretion of the dye with the bile, (3) patency of the hepatic and cystic ducts, (4) a properly functioning resistance mechanism at the terminus of the common bile duct, and (5) ability of the cystic mucosa to concentrate the bile. With all these factors normal, disease of the biliary tract would reasonably seem to be excluded; yet, so far as the gall bladder is concerned, they practically signify only that this viscus is able to receive and concentrate bile. It is true that disease usually interferes with one or the other function, and since cholecystographic diagnosis is based almost solely on alteration of these functions, errors are bound to occur.

It is generally accepted that a normal series of cholecystograms is one which exhibits a definite, homogeneous, clearly outlined shadow of the gall bladder, the shadow varying in size and having a tendency to diminish at succeeding examinations or after a meal rich in fats. No standard size can be prescribed as normal, for the bile-content varies considerably during the fasting state, and unless the gall bladder is extremely large or fails to contract after a fatty meal its size is not of significance. Experience indicates also that, with the oral method at least, no certain degree of density can be fixed on as normal, but that the density varies widely within normal limits, and, unless the shadow is extremely faint throughout the series, the response should be considered normal. The personal equation enters inevitably into the discrimination between faint and normal shadows, but after checking roentgenologic with surgical data the examiner will become cautious in adjudging any shadow to be faint.

Another element which may affect the examiner's judgment is the clinical history. In the first instance the cholecystogram should be interpreted without any knowledge whatever of the clinical facts; otherwise the diagnostic opinion will be influenced. The final clinical diagnosis should rest on a correlation of all the facts by the clinician, alone or in conference with the roentgenologist, but the tentative roentgenologic diagnosis ought to be based solely on the cholecystograms.

To estimate the diagnostic accuracy of the normal cholecystogram I have reviewed 251 cases examined during the current year at the Mayo Clinic, with a normal response, in all of which surgical exploration was carried out. The gall bladder was found to be

[1]Read before the Radiological Society of North America, at New Orleans, Louisiana, December 1, 1927.

normal in 204 cases, thus confirming the roentgenologic report in approximately 81 per cent of the series. Lesions found in the 204 cases were as follows:

	Cases
Duodenal ulcer	78
Gastric ulcer	5
Gastric and duodenal ulcer	5
Gastrojejunal ulcer or mal-functioning gastro-enteric stoma	3
Gastric carcinoma	2
Hepatic carcinoma	1
Pelvic lesion	34
Chronic appendicitis; carcinoma of colon; diaphragmatic hernia, or other abdominal lesion	75
None	1

In this group of gall bladders that were normal both roentgenologically and surgically, localized hepatitis and enlarged lymph nodes were found in 27 instances, and adhesions to the gall bladder in 40, the viscus being buried in adhesions in many cases. On the other hand, I have seen many cases in which the shadow of the gall bladder on the cholecystogram was deformed or serrated, although at operation no adhesions or deformities of contour were present. The conclusion seems inescapable that attempts to diagnose pericholecystic abnormalities by cholecystography will usually lead to embarrassment and failure.

It is interesting also to note that, although the gall bladder is suspected to be a temperamental organ and easily subject to reflex disturbance, it was not affected, at least from the roentgenologic viewpoint, in 204 cases, in all but one of which there was marked disease of abdominal organs. Duodenal ulcer especially has been assigned as a cause of disturbed function of the gall bladder, yet in 78 cases of duodenal ulcer and in 5 of associated gastric and duodenal ulcer the cholecystograms were normal.

In 37 cases, or nearly 15 per cent of the 251 cases, definite cholecystitis without stones was discovered at operation. In this sub-group the cholecystograms were normal in every respect, and even when the films were reviewed in the light of the anatomic data no abnormality of the shadows could be discerned. This group represents what has been, in my experience, an inevitable source of error.

There remains a small sub-group of 10 cases, slightly less than 4 per cent of the series, in which cholecystitis with stones was found at operation. The concretions were small in most instances and few in number, but some of them were fairly large. To ordinary view the cholecystograms were apparently normal and had been reported as negative. On careful re-inspection, however, one or two rather minute translucent areas could be seen in the shadow of the gall bladder in seven cases. If these areas had been observed originally, the examiner would probably have attributed them to gas in the bowel which was obvious in most instances. Nevertheless, if re-examination had been asked for, these errors might have been avoided. As it is, the errors should now be charged to the examiner rather than to the method. In the 3 remaining cases of the 10, restudy of the films failed to disclose any abnormality.

If conclusions may be drawn from this series they would be as follows:

1. Positive cholecystographic diagnoses have a higher percentage of accuracy than negative diagnoses.

2. Cholecystitis without stones is not incompatible with a normal cholecystogram, and the percentage of normal responses in such cases is probably higher than is generally believed.

3. The normal cholecystographic response is at its best in ruling out gallstones. The stones are usually manifested as translucent spots that are most often obvious and

characteristic by reason of their size, number, and configuration, but in a small minority of cases the rarefactions are so minute and so few that careful scrutiny is requisite to discern them. In all doubtful cases of this character, a second examination should be made.

4. While the gall bladder is believed to be sensitive to autonomic nervous influences, its behavior in the cholecystogram, as observed in this series, is apparently seldom affected by duodenal ulcer, chronic appendicitis, pelvic lesions and many other diseases of abdominal organs.

GALL AND GALL-BLADDER DIAGNOSIS[1]

A CRITICAL REVIEW OF THE ROENTGENOLOGICAL DIAGNOSIS OF GALL-BLADDER DISEASE

By I. S. HIRSCH, M.D., and H. K. TAYLOR, M.D., NEW YORK

IT was only after the technic of the roentgen examination of the gastro-intestinal tract had been considerably elaborated that the studies of the gall-bladder region began to yield results which had a dependable significance.

True, there had been sporadic and isolated demonstrations of gallstones many years previous to this, as far back as 1900. In those ancient beginnings, Beck (1) labored with primitive apparatus and long exposures to detect biliary calculi. With the limited means then available he did succeed in two cases in showing calcium calculi. But his results and those given in the desultory reports by Kohler (1904), Mikulicz (1905), Mathias and Fett (1909), Pfahler (1910), Haenisch (1910), Holland (1913), Cole (1914) were not such as to indicate that the method was sufficiently reliable to warrant its establishment as reliable routine examination.

In 1913 (2), however, following reports in which calculi and gall-bladder disease were diagnosed by direct and indirect criteria, there was initiated a period of great activity of radiological research, mostly on the part of American workers, for the determination of the roentgen criteria of gall-bladder disease.

The problem centered about two points: one the detection of calculi and the other the morphological and physiological changes in the viscera related anatomically and physiologically to the gall bladder. Of the delineation of the gall bladder itself there was as yet no inkling.

That the methods of examination and the criteria on which the diagnoses were based were still insufficient was made continually apparent by the marked discrepancies in the results obtained by various observers.

The claims in regard to the possibility of the detection of gallstones were as numerous and varied as the workers who submitted them. Some enthusiasts, unabashed by the small number of cases on which their statistics were based, claimed correct demonstration in 75 per cent of the cases. On the other hand there were others who despairingly bewailed their impotence, in that operative results disclosed that calculi could be detected in only about 20 per cent of cases.

When, however, further experience proved that the optimistic estimate was not warranted and that 30 per cent was a more accurate figure, the scope of the diagnosis was sufficiently generalized to meet the needs of the particular maker of statistics. The diagnosis was now no longer "positive or negative to biliary calculi." The roentgen findings were now registered under the heading of "pathologic gall bladders." The conclusions which frequently comprised such diagnosis as "the evidence is consistent with gall-bladder disease," which is an equivocation and not a diagnosis, arrived at by considering every possible clue, sign, and symptom, resulted in the production of a series of statistics in which the diagnosis was perilously near the maximum, barely allowing for the possibility of human error.

Such results, however, created in the minds of those who carefully analyzed the problem, doubts which would not down. It was evident that the criteria on which such diagnoses were based were not all of them

[1]Presented before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

signs having any pathologic import. Many were normal appearances or obtainable in normal individuals with no symptoms referable to the gastro-intestinal tract or gall bladder. Among such radiological signs may be mentioned irregularity of right diaphragm, rapid rate of discharge from bulb, close proximity of colon to gall bladder, variation in position of the second part of the duodenum, fixation of the jejunum in right upper quadrant, dilated duodenum distal to bulb, pressure on antrum or bulb. Other signs on which much stress was laid as important criteria for the diagnosis of pathologic gall bladder were the local or general evidences of spasm, *viz.*: tubular or spastic antrum, gastric hypertony and hyperperistalsis, the displacement of the pylorus, displaced bulb, irregularity in the contour of the bulb, and gastric retention —signs more often due to other diseases than those of the gall bladder.

To these, a certain school added a sign which they considered pathognomonic—the visualized gall-bladder shadow. Upon this sign they laid tremendous emphasis. According to this school a normal gall bladder could not be visualized. Only when some pathologic change had taken place in the walls of the gall bladder or its contents could its shadow be demonstrated.

A study of the histories of the cases making up these reports discloses the fact that the cases operated on all had many definite symptoms typical and characteristic of gall-bladder disease. In fact, the clinical picture was so evident and striking as to make the surgical indications clear. The X-ray examination, even if in the negative, would not have prevented operation and the positive roentgenographic findings, such as they were, were merely corroborative. Here, then, we have a condition of affairs in which a study of cases, clinically diagnosed as gall-bladder disease, yields, by a laboratory test, a high percentage of correct diagnoses, irrespective of the data on which the diagnoses are based.

But now, an able and alert pathologist, on the basis of extensive material, published a report of the pathologic examination of 4,998 gall bladders removed on the basis of clinical criteria in which 96.5 per cent showed definite pathologic changes on microscopic examination (3, 4). It must be conceded that such reports are of fundamental value in that they furnish a basis on which to evaluate the roentgen examination. If the clinical symptomatology of gall-bladder disease is so definite and clear that the operation based on such criteria shows such a high percentage of corroboration, what need is there of any laboratory method? Why should the results of any laboratory method be a source of jubilation? By any roentgen technic and on the basis of any roentgen criteria, the percentage of correct diagnoses as checked by operative findings, must be above 90 per cent. This seems to have cleared the atmosphere for a time from the bewildering fog of statistics which obscured the problem.

For a period, therefore, the status of the X-ray examination of the gall bladder seemed to have returned to a rational basis. The aim appeared to be a surer delineation of calculi, and a determination of the severity of the direct and reflex effects of gall-bladder disease on the gastro-intestinal tract.

This was the state of affairs until the advent three years ago of a new method which permits a clear visualization of the gall bladder, by the administration of tetraiodophenolphthalein (5).

The liver secretes the dye into the bladder in varying amounts and concentration, and the integrity of the gall bladder is judged on its ability to fill, to concentrate, and to evacuate. And now on the basis of new catch phrases, "no shadow," "delayed shadow," and "faint shadow," there has begun

an orgy of statistical figure-juggling which puts the old pre-dye statisticians to shame. And as the new and highly enthusiastic group blow their trumpets and beat their drums, the ancient calculators sit sulking in their tents. Truly here is a brood of their own engendering. Here are statistics with percentages as good and better than those they flaunted.

Thus, as to the value of the signs (6), the following statistics of the correctness of the cholecystographic findings are given:

Description	No. of cases	Percentage correct
No shadow	9	100
Persistency of shadow	16	75
Faint shadow	18	100
Late appearance of shadow	1	100
Gall-bladder shadow without dye	9	100
Gallstones with dye	26	91
Gallstones without dye	8	100
Pathologic gall bladder with stones	34	93
Pathologic gall bladder without stones	26	0
Total cases reported negative	40	100
Total cases reported pathologic with or without stones	60	91
Deformity	6	no operation
Adhesions between gall bladder and duodenum	11	75
Adhesions between gall bladder and colon	5	100

Thus the following criteria are infallible (100 per cent):

No shadow

Faint shadow

Late appearance of shadow

Negative reports

Adhesions reports

From such results it is justifiable to infer that we have reached the desired goal. From such results and on the basis of such calculations it is made to appear that "no shadow, delayed shadow, and faint shadow" is a diagnostic slogan which comprises the whole truth of the problem of the detection of gall-bladder disease. The signs "no shadow, delayed shadow and faint shadow" have a value of 100 per cent and the negative value of the test is infallible (100 per cent).

When, however, this table of results is analyzed it is found that the basis of these high percentages is entirely unjustified from a clinical and scientific viewpoint. The figures are deduced from too few cases. Thus—

Late appearance of gall-bladder shadow	1 case
Operated on	1 case
Correct	1 case
Percentage	100
Persistence of shadow	16 cases
Operated on	4 cases
Correct	3 cases
Percentage	75
No shadow	9 cases
Operated on	7 cases
Correct	7 cases
Percentage	100

The negative value of the method—

Total cases reported negative	40 cases
Operated on	1 case
Correct	1 case
Percentage	100

The 100 per cent correct diagnosis of adhesions between gall bladder and colon is based on one case operated upon.

In an article on cholecystography, Graham (7) tabulates cases reported in the literature in which the cholecystographic examination has been checked by operative findings.

Author	Method of administration	Diagnosis of normal gall bladder: Normal gall bladder at operation	Diagnosis of normal gall bladder: Pathologic gall bladder at operation	Percentage of correctness of cholecystography
Cohen and Roberts	Intravenous	2	0	100
Stewart and Ryan	Oral	1	0	100
Jewett	Oral	2	0	100
Winslow and Melgard	Intravenous	1	0	100
Nemours-Auguste	Intravenous	3	0	100
Kaznelson and Reimann	Intravenous	1	0	100
McCoy and Graham	Intravenous	8	0	100
Gosset and Lowey	Mostly intravenous	21	0	100

Here are the "hundred-percenters" in the forefront again. In the preceding table, in-

tended to indicate the great value of negative report, there are eight 100 per cent reports out of a total of 12 reports; 6 of these 8 are based on 3 cases or less, one on 8 cases, and one on 21 cases. Yet Carman's examinations of 48 cases gave a percentage of correctness of the negative diagnosis as about 44 per cent.

Were the criteria[2] for the establishment of a definite positive or negative diagnosis of pathology by the cholecystographic method firmly and definitely established there might be some justification for a summary on the part of Graham in the conclusion that a pathologic gall bladder is correctly diagnosed in 97.8 per cent and a normal gall bladder in 74 per cent, and that the intravenous method is accurate 95 per cent and the oral 89 per cent. Surely such summary is not as yet justified, for there is by no means any unanimity of opinion as to the best technic or most reliable criteria. Each observer imagines that his success is due to a particular technic, one to his method of preparation of the patient, another to his method of preparing the capsules, another to the particular sequence of his examination, and each examiner also imagines that his success is due to his particular skill in judging findings. A critical analysis of the literature shows that the emphasis placed by many on these criteria is by no means justified.

ABSENCE OF SHADOW OF GALL BLADDER

The absence of gall-bladder shadow has not always the significance of indicating a pathologic gall bladder. Nor does the mere fact that no shadow can be detected prove that bile is not present in the bladder. In fact, the gall bladder may be distended with bile. Yet it is, by the statistics quoted, the best and most infallible sign of gall-bladder disease. When the examination is made intravenously it is said to be certain, indicating an obstructive lesion; when the dye has been given by mouth it is said to be suggestive but demanding corroboration. Although the test made by the oral method may show no gall-bladder shadow, it may perhaps be shown by the intravenous method. Even if repeatedly it fails to show by the oral method or by the intravenous method, the gall bladder may still be found normal. There may be no shadow even with a perfectly free cystic duct regardless of the condition of the gall bladder. In many of the cases in which the gall bladder is not visualized there are calculi which (not obstructing the cystic duct) may or may not be seen on the film. There may be no filling of the gall bladder and yet at operation a duodenal ulcer or gall-bladder adhesion without actual gall-bladder disease may be found. Even in the presence of calculi the gall bladder may fill and empty normally. All that can be inferred from a continued absence of shadow is that there is an impairment of the interchanges of bile in the gall bladder. According to Graham it is a fact of great significance that the normal gall bladder is never found empty. Yet just before the advent of the dye method a high percentage of pathologic gall bladders were correctly diagnosed (as checked by operative findings) on the basis of a visualized gall-bladder shadow. On one hand, therefore, in pre-dye days the visualized gall bladder was the *hoc signo vincis* and now in this new dynasty it is the non-visualized gall bladder which is the blazing sign.

Delayed shadow of the gall bladder.—A delay in the filling of the gall bladder with dye or the late appearance of the shadow is not of any important significance. There are too many factors, any one of which can account for this. Not one of these factors can be considered as a criterion pointing to-

[2] The various criteria on which the diagnosis is based are the same in the oral and intravenous administration of the dye. Only the time sequence of the taking of the roentgenograms differs.

wards a pathologic gall bladder. Rapid passage of the dye through the intestinal tract, considerable mucus in the alimentary canal, insolubility of the capsule or pill coating—any factor preventing absorption—will cause a delay in the appearance of the gall-bladder shadow. So also diseases of the liver interfering with its function and producing a diminished bile supply and incomplete obstructive lesions of the hepatic ducts may be responsible for a delay in the appearance of the gall-bladder shadow. Besides this there are individual reactions to the dye which are not sufficiently considered.

FAINT SHADOW OF GALL BLADDER

No inference can be drawn from density of the shadow at the first examination. Actually this is dependent on the quantity of the dye within the gall bladder, and it is inconceivable that there may not be normally a considerable variation in this quantity. The density of the shadow is also dependent on certain factors, many of which are of no pathologic significance.[3] Nor is the concentrating power as judged between the first and second examination of any value as an index. When concentration is apparent it is a normal finding. When it is absent very little or no significance can be attached to it. In a general way it may be stated that one of every two gall bladders which fill normally may be pathologic. Or, to be more exact, out of every 100 pathologic gall bladders, 40 will show a dense shadow, 40 will show no shadow, and 20 will show a shadow which has not the maximum density.

The highest concentration measured by a color standard was given by a gall bladder which was most diseased (a gall bladder with a thin wall, atrophic mucosa, epithelium one-half denuded and with cellular infiltration in the wall (8). Yet Moore states that the real purpose of cholecystography should be as a measure of concentrating capacity of the gall bladder. As the maximum, therefore, even when judged by color standards, incomplete concentration means pathology in only 20 per cent.

Among the other signs which are much vaunted is the delayed evacuation of the dye. This is said to indicate a disturbance of motor activities of the gall bladder and, therefore, to be a sign of disease. It might have some significance could physiologists agree as to the method by which the gall bladder empties. Is the dye expelled through the cystic duct or is it absorbed through the lymphatics? Though there is definite musculature in the gall-bladder wall, still no one has ever seen gall-bladder peristalsis. The change in conformation and the reduction in size of the gall-bladder shadow after a meal, is greater in the width than in the length, until the very last stage of evacuation, which would suggest a slow continuous tonic contraction, which, even under normal conditions, may not completely evacuate the dye in three hours. It has been shown that even severe disease of the mucous membrane does not affect concentration by interfering with the absorption of water and salts. Why then should it interfere with the absorption of the dye? Then, too, there is, undoubtedly, a resecretion of the dye into the gall bladder after evacuation and this contributes to the apparent complete evacuation of the dye. Under these circumstances the symptom is of no value. In the majority of cases reported in which there was delayed emptying (residue at 2½ hours *p. c.*), the gall bladder was normal.

The significance of the morphological deviations from the normal (excluding the rare congenital anomalies, etc.) cannot as yet be formulated, because a normal morphology and its variations (by this is meant the living morphology as determined by roentgen studies) has not as yet been es-

[3] A slight change in exposure time, a variation in target film distance, a different intensifying screen, a variation in the make of film, a change in developing time, etc., will produce a varying density of gall-bladder shadow.

tablished. The relationship between the morphology of the gall bladder (size, shape, contour, position, and mobility) and habitus, when finally formulated, may contribute to the diagnostic problem.

The so-called deformities of the gall-bladder outline due to adhesions cannot be substantiated by operative scrutiny. The study of the gall-bladder shadow itself is not sufficient for the determination of such pathologic changes. The relationship between the bladder and the adjacent viscera must be examined. On the other hand, such signs as the crescentic deformity of the duodenum, on which so much stress was laid, is now known as a sign of no pathologic import. Scarcely 10 per cent of the adhesions involving the gall bladder can be determined by cholecystography alone.

CALCULI

To the surgeon the presence of calculi is a clear indication for operation. That the importance of this finding outweighs, in the surgical mind, any of the other data obtainable by the dye test is clearly apparent from a study of the statistics. Thus, in Stewart and Ryan's statistics gallstones were detected without dye in 8 cases, with the dye in 26 cases, making a total of gallstones detected, 34 cases. These are classified as follows:

Pathologic gall bladder with stones	34
Operated upon	15
Correct	14
Percentage correct	93

But where no stones were present and a pathologic gall bladder was reported, there were 26 cases of which *but one* was operated on, and that found normal. In all, therefore, a pathologic gall bladder was reported in 60 cases; 23 of these 60 were operated upon, and stones were found in 14, or about 60 per cent.

In Graham's statistics only 147 cases out of 1,246 examined, a little more than 12 per cent, were operated upon, proving that the surgeon and clinician select, isolate, and determine the cases in which indication for operation exists, in spite of roentgen findings.

The contribution of cholecystography to the detection of calculi is based on two findings: "mottling" (irregularity in the density of the gall-bladder shadow) and "negative shadows."

An irregularity in the density of a gall-bladder shadow is supposed to be always due to small biliary calculi. It may be due, however, to folds in the mucous membrane or to filled Rokitansky-Aschoff sinuses. The mucous membrane in a collapsed gall bladder shows numerous folds or rugæ. As the gall bladder fills and the pressure increases these folds are smoothed out. In a partially filled gall bladder where the rugæ are not entirely obliterated, the folds of mucous membrane may displace a certain amount of the dyed gall and produce variations in the density of the shadow.

Soft biliary calculi which do not cast a shadow without the dye are evidenced as "negative shadows," merely by displacing a given quantity of bile. There are many instances, however, where soft bilary calculi are present and are not so shown. In some instances these may be demonstrated shortly after the "evacuation meal" before there is complete emptying of the dyed gall. When the emptying of the dyed gall is completed these calculi will not be detected. It is thus clearly apparent that all soft calculi cannot be detected, no matter what routine may be used. "Negative shadows" must be definite. If there is merely a suspicion of their existence, the finding is of no significance. In spite of all this, the production of "mottling" and "negative shadows" has increased the percentage findings of calculi. On the other hand, a certain percentage of biliary calculi, those with a calcified periphery

which are demonstrable without the dye, may be entirely obscured by cholecystography. For this reason roentgenograms of the gall-bladder region must be made before administration of the dye.

It is apparent that the diagnosis of stone has been improved but not made infallible by cholecystography. There are still stones which escape detection, and, when the percentage of increased errors due to the diagnosis of calculi on the basis of "mottling" and "negative shadows" is added, the actual percentage of calculi detectable is not above 60 per cent.

In reviewing the whole problem of the diagnosis of gall-bladder disease one is driven to the conclusion that cases of the type which give a definite clinical history and symptoms of cholecystic disease (pain under the right costal margin radiating to back and right shoulder, periodic attacks associated with nausea and vomiting, eructation after meals, and jaundice with clay-colored stools) have always been diagnosed correctly by every method—by clinical[4] study, by indirect roentgenologic signs, direct roentgenologic signs, and cholecystography. And the reports of the pathologists as to the percentage of pathologic gall bladders properly operated upon, on the basis of the criteria of clinical phenomena and cholecystography, has not yet increased as a result of this new method.

But now, another change of front is becoming apparent! Another realignment is beginning to take shape. At first like a mere mist, shadowy and indefinite, it has actually assumed the form of clear expression. It is this, that the greatest value of the cholecystographic examination lies in the study of disturbed physiology. The absence of gross pathologic lesion in cases found negative at operation indicates merely that organic changes have not as yet appeared. There is, nevertheless, present in these cases such a disturbance of the function as will lead to a certain definite organic change in the gall bladder, and that such gall bladders are properly removed. The danger of such a point is evident, the tendency alarming. Are we approaching an era similar to that, happily passing, in reference to the appendix, when the gall bladder is to be removed on a dubious pretext? There was an era when the appendix was removed because it was considered responsible for certain gastro-intestinal symptoms; and now, when the numerous cases with recurring symptoms are raising the question whether the appendix was really the sinning organ, the odium of guilt is to be passed on to the gall bladder. Are the clinical results after cholecystectomy in these cases an indication that the operation was justified? The same reaction is obtained for a period after the appendix operations. Some observers have already gone so far in this opinion as to maintain that every individual with dyspeptic symptoms, in whom the slightest disturbance in the sequence of events in the dye test appears, should be submitted to operation.

In a group of 52 patients (9), a majority of whom gave *very indefinite* gastric symptoms, the history and cholecystographic evidence of abnormality was sufficient justification for operation. The cholecystographic evidence was based on the "faint shadow, delayed shadow, and no shadow" slogan. On the basis of these signs the 52 gall bladders were removed. In all of these cases the mucosa was found intact. By microscopic examination, however, in most of the cases lymphocytic infiltration was found, and the explanation, rationalization, and justification for the operation is that, although the gall bladder may grossly show little or no pathology, such gall bladders are not functioning normally and should be considered pathologic. This startling viewpoint

[4] In 90 per cent of all cases of cholecystitis and cholelithiasis a correct diagnosis can be made from the history alone.—W. H. Bodenstab, Jour. Am. Med. Assn., July 6, 1918, LXXI, 12.

is arrived at by the author quite independently of the similar conclusion of Graham and his associates.

CONCLUSIONS

It is a fact worthy of note that in the three years since the publication of the first paper on cholecystography by Graham and Cole, the diagnostic value of the procedure has not yet been standardized. There exists a feeling of uncertainty regarding the extent of its value and the criteria by which a diagnosis is to be established. At first advanced and intended primarily as a diagnostic aid superior to every other method in determining organic changes, it now has come to stand as a method of studying disturbed function.

On one point, however, there seems to be unanimity—that it has increased the percentage of calculi detectable and as such it may be of extreme value in the treatment of the early stages of gall bladder disease.

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ON THE RELATIONSHIP OF GALL-BLADDER EMPTYING TO INGESTED FATS[1]

By DANIEL N. SILVERMAN, M.D., and WILLY DENIS, Ph.D., New Orleans

As the result of a series of experiments made on cats the fact was first pointed out by Boyden (1), at the Boston meeting of the American Association for the Advancement of Science, in 1922, that the ingestion of a mixture of egg yolk and cream caused a rapid expulsion of bile from the gall bladder. On the publication by Graham and Cole (2) of their method for the visualization of the human gall bladder, Silverman and Menville (3) at once applied this technic to a study of gall-bladder emptying by the intraduodenal instillation of magnesium sulphate solution. The results showed that the gall bladder emptied when repeated injections of this chemical were made into the duodenum. Subsequently, Boyden (4) made a study of the problem and was able to show by experiments made on himself that in the human subject the administration of the yolk of four raw eggs and a half-pint of cream caused a rapid expulsion of bile, a phenomenon which was not noted when lean meat or carbohydrate was eaten. The experiments of Boyden led him to believe that the egg yolk was more efficient in causing expulsion of bile than the cream, and he therefore carried out experiments with cats in which substances containing preponderating amounts of the three lipoids known to occur in the egg yolk (neutral fat, lecithin, and cholesterol) were present. For this purpose he used lard, lecithin (Merck), and lanolin, each of these substances being fed to the animals by means of a stomach tube, both with and without cream. The results obtained indicated that lecithin was most active.

In a later series of experiments (5), however, with samples of lecithin as prepared by Eastman and used in the Harvard laboratories, it was found that the administration of this substance failed to cause complete emptying of the gall bladder. This finding has caused Boyden to discard the theory that this body is the specific substance responsible for the effect of egg yolk.

The initial findings of Boyden have received corroboration at the hands of numerous investigators, an excellent discussion of whose work is to be found in the recent paper of Hamrick (6). It therefore need not be discussed here.

As regards the mechanism of the stimulation of the gall bladder by ingested egg yolk, the question arises not only as to what constituent of this food is the active principle but also as to how it effects the desired result, whether by a hormonal type of action due to the absorption of some constituent or product of digestion into the blood stream, or due to the presence in the duodenum of the egg yolk itself or some digestion product produced therefrom. In his latest work Boyden (5) states that his experimental results "indicate that the gall-bladder musculature does not respond to the presence of food in the gastro-intestinal tract unless digestion and absorption have occurred," and that "the gall bladder is subject to both nerve and hormone control."

In this paper we wish to present the results of a series of experiments in the course of study of the effect of the administration of various lipoids, with especial reference to the factor of absorption on the gall bladder by means of the visualization method of Graham and Cole. The work was carried out on persons who, so far as it was possible to determine, had no abnormality of the

[1]From the Department of Medicine and of Biochemistry of the School of Medicine, Tulane University, New Orleans. Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

X-ray No.	Date	Mgm. total fat per 100 c.c. blood						Fat given.	Comments
		Fest'g	30 min.	45 min.	1 hr.	1½ hr.	2 hrs.		
68742	May 25	832		832		895		Cream oz. 2 Egg yolks 2	Visualization satisfactory; gall-bladder shadow disappeared in 45 minutes.
68779	May 27	908		972		980		As above	Visualization satisfactory; gall bladder emptied 50 per cent end of 45 min.; end of 90 min. shadow greatly reduced, not completely empty.
68926	June 1	862	862	865				Cream oz. 4	Cream given after Plate II; 30 min. after cream shadow appreciably reduced; 45 min. after about 50 per cent reduced.
71026	Sept. 12	866			855		1178	As above	Over 50 per cent reduction in shadow one hour after cream; complete disappearance after two hours.
71108	Sept. 16	1350			1285		1240	Egg yolks 3	Visualization good, shadow reduced 50 per cent end of one hour. Complete disappearance at end of two hours.
71131 No. 2	Sept. 17	860					890	As above	Visualization good. At end of one hour shadow reduced two-thirds; end of two hours further slight reduction, but not complete disappearance of shadow.
71293	Sept. 21	814			920		937	Olive oil oz. 1	Visualization fair only; no reduction one hour after oil and slight after two hours.
71323	Sept. 23	1142			1171		1220	Total egg lipoid grams 20	Visualization good. No reduction in shadow one hour after. Appreciable reduction after two hours.
71355	Sept. 26	1035			1048			As above	Visualization fair. Total disappearance of shadow at end of one hour.
71694	Oct. 12	820			825		828	As above	Visualization satisfactory; reduction 50 per cent end one hour; about complete end two hours.
71802	Oct. 19	977			1010		1550	Lecithin grams 10	Visualization fair. Marked reduction in shadow end one hour. Slight further reduction end of two hours.
71803	Oct. 19	1023			1050		1060	As above	Visualization very good. Reduction 50 per cent end of one hour; further reduction at end of two hours.

gall bladder. The method of procedure in all cases was as follows: The gall bladder was visualized by the oral administration of tetraiodophenolphthalein. The subject, while fasting, was bled immediately following a satisfactory visualization, usually from 14 to 16 hours after dye administration.

In order to determine if possible whether absorption of lipoid had occurred, 5 c.c. samples of blood were obtained by vein puncture at appropriate intervals after the administration of the lipoid-containing substances. These were analyzed for total fatty acids by the method of Bloor, Pelkan, and Allen (7), and, in a few instances, for lecithin by the procedure of Whitehorn (8).

In referring to the accompanying chart it is noted that the ingestion of cream and egg yolk mixture, cream and egg yolk separately, or the constituents of egg yolk (total lipoids or lecithin) produces appreciable emptying of the gall bladder. The non-emulsified fat (olive oil) had practically no effect on the gall-bladder shadow. These findings are in accord with the results published by Boyden.

In neither of the cases examined was there a great increase of the blood fat at the time that the gall bladder was emptying; in fact, very slight rises in the blood fat or no rise at all were determined in the individuals showing most marked emptying of the gall bladder.

CONCLUSIONS

While emulsified fats when ingested produce emptying of the functioning gall bladder, our experiments suggest that the factor of absorption of digested fat bears no relationship to the emptying of the gall bladder.

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CHOLECYSTOGRAPHY IN THE LATE MONTHS OF PREGNANCY[1]

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IT IS a well accepted clinical and pathologic fact that gall-bladder disease occurs more frequently in women who have borne children than in those who have not. Very often the initial attack of cholecystitis or cholelithiasis is inaugurated during the course of an otherwise normal pregnancy.

Numerous etiological factors have been advanced for the inception of biliary tract disease such as infection of the biliary radicles and gall bladder, increased cholesterol content of the blood with a deposit of cholesterol in the gall bladder, stagnation of bile due to interference with the neuromuscular control of the sphincter of Oddi, visceroptosis, the wearing of tightly fitting corsets, pressure due to the enlarging gravid uterus, lack of exercise, indiscretions of diet, and chronic constipation.

Those causes that are considered to be related to pregnancy are morning sickness, cholesterinemia, pressure of the enlarged uterus on the liver and gall bladder, alterations in the constituents of the bile resulting in its inspissation, with precipitation of cholesterin. The rôle of infection in conjunction with these has been emphasized by a number of students of the subject.

With the advent of cholecystography, we felt it might be possible to show in a group of pregnant women what alterations in size, shape, position, and function of the gall bladder occur during this period and their relationship to cholecystic disease.

PROCEDURE

A non-biliary stimulating meal was given at 5 P. M. At 8 P. M., three grams of tetraiodo in 100 cubic centimeters of distilled water were administered intravenously by the gravity method, fifteen minutes being consumed in this procedure. Patients presented themselves for X-ray examination fourteen hours later, breakfast having been omitted. With the patients in the prone and upright positions, three radiographs were made during the first hour. In each instance where visualization resulted, a Boyden meal (egg yolk and cream) was administered immediately after the last exposure and further examinations were conducted, beginning one hour later.

Bearing in mind that in order to secure a shadow it is essential that sufficient dye be excreted by the liver into the bile, which, in turn, must enter the gall bladder, there to be concentrated, it is obvious that interference with liver secretion, blocking of the ducts, pathology involving the gall bladder, or inability of the dye to displace the thickened contents will result in impaired visualization or interference with concentration.

It has been shown that the liver possesses a large margin of safety, a small portion of normal hepatic tissue being able to carry on adequate function. In order that interference with visualization might not be attributed to the inability of the liver to excrete the dye, seventeen selected primiparæ in whom we were unable to elicit the existence of any biliary tract disease by history or physical examination were studied by the Graham method.

Analysis of this series of cases presents many observations which warrant consideration and justify certain conclusions.

VISUALIZED GROUP

In ten of the cases in which visualization occurred there was no delay in time of the

[1]Read for the authors before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, December 1, 1927.

appearance of the shadows, which were of homogeneous density. Response to the Boyden meal was prompt, adequate diminution in some to complete disappearance of the shadows in others taking place during the first, second, and third hours following ingestion of egg yolk and cream. These facts warrant our placing this group of ten cases in the category of the normal.

Size, Shape, and Position.—It is interesting to observe the size, shape, and position of the gall bladder in different types of non-pregnant women. Most text-books of anatomy describe it as about three inches long by one and one-fourth inch in diameter and as generally being pear-shaped, with its fundus lying near the end of the ninth costal cartilage. Cholecystography in normal adults has revealed marked variations from the usual anatomical description. It is seen to be from one to five inches in length and from one to three inches in diameter. It is oval, globular, pear-shaped, or crescentic. It has a wide range of mobility and not infrequently the fundus is below the level of the crest of the ilium. It may occupy any position between the costal margin and the crest. Its inner border may approximate the spine or be several inches distant from it.

The visceral topography, however, is dependent upon the habitus—well up under the right costal margin in the broad type and low in position in the enteroptotic. We were able to demonstrate that the gall bladder can be pushed upward, outward and to the right with distortion of its contour by the enlarging uterus which encroaches upon the hepatic region. The gall bladder occupied a high position in all of the visualized group of our cases, regardless of the bodily habitus. Considering that seven were of the enteroptotic type in which the gall bladder would be expected to be low-lying, it is apparent that the size of the uterus in the late months of pregnancy causes a definite upward displacement of the gall bladder.

The size of the viscus is not perceptibly altered during pregnancy, there being no variation from that noted in non-pregnant women.

Definite pressure defects producing some degree of distortion were encountered in six of the ten visualized cases, the shadows pre-

TABLE I

VISUALIZED GROUP

Case No.	Weight (pounds)	Height (inches)	Distance Above Level of Crest of Ilium (inches)	Pressure Deformity	Boyden Response	Degree of Concentration
1	122	61	6	Present	Normal	++++
2	114	63	7¾	Absent	Normal	+++
3	140	64	3¼	Absent	Normal	++++
5	125	64	7½	Absent	Normal	+++
6	127	62	6⅜	Present	Normal	+++
9	119	60	6¾	Present	Normal	+++
10	122	63	3¾	Present	Normal	++++
12	122	64	6¼	Present	Normal	++++
13	145	64	5¼	Absent	Normal	++++
14	136	62.5	6	Present	Normal	++++

senting irregularity of contour in some instances and appearing flattened in others.

As is well known, alterations in the position of the liver and the gall bladder due to visceroptosis, external or internal pressure have been accepted as etiological factors in the production of biliary tract disease. This alteration in shape and position thus may interfere with the emptying of the gall bladder, produce stasis of its contents, which, with the increased bile cholesterol of pregnancy, forms a thick inspissated content which the dye cannot displace, and consequently no shadow be obtained.

NON-VISUALIZED GROUP

Seven of the seventeen cases failed to visualize. No calculi were seen in any. The position of the fetus demonstrated that the uterus approximated the liver and gall-bladder region. Owing to the fact that in the ten visualized cases the uterus occupied a similar position, we do not believe that mechanical pressure and distortion alone are responsible for shadow failures and cannot uphold the contention that the enlarging uterus *per se* is an etiological factor in biliary tract disease.

From Table II it is evident that only two of the non-visualized group were free from morning sickness, while in the visualized, six were free. It is difficult in this small number to interpret the significance of this disproportion. Nevertheless, it is obvious that morning sickness occurred more frequently in the non-visualized group.

CASE REPORTS

Owing to the pregnancies, it was necessary in the interpretation of the shadows to formulate personal standards as to degree of density.

Visualized Group

Case No. 1, S. J., eighth month of pregnancy. Age 18, weight 122 pounds, height 61 inches. Urine and Wassermann negative. Blood pressure 140/80. No morning sickness during entire course of pregnancy.

Cholecystographic findings, August 31, 1927: Gall bladder visualized, degree of concentration ++++, pressure defect of the fundus, which was 3¼ inches distant from middle of first lumbar vertebra and 6 inches above the highest point of the iliac crest. During the first hour, the shape changed from globular to oval. There was a normal Boyden meal response. The buttocks of the fetus approximated the fundus of the gall bladder.

Normal delivery and child, September 23, 1927.

Case No. 2, D. L., seventh month of pregnancy. Age 19, weight 114 pounds, height 63 inches. Urine and Wassermann

TABLE II.—MORNING SICKNESS

Visualized Group		Non-visualized Group	
Number of Cases	Duration of Sickness	Number of Cases	Duration of Sickness
1	2 Months	2	2 Months
2	3 Months	2	3 Months
1	6 Months	1	9 Months
6	0 Months	2	0 Months

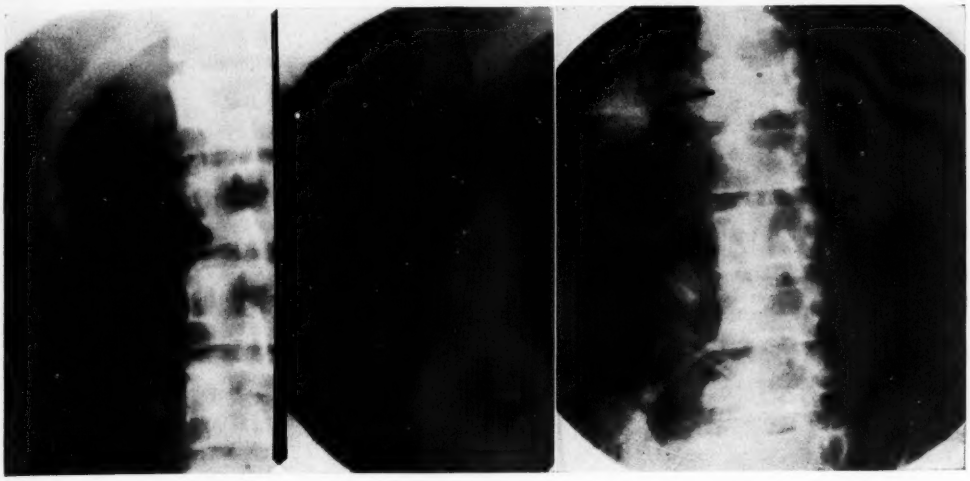

Fig. 1. (*A*) Fourteen hours after injection of dye. (*B*) One hour after ingestion of Boyden meal, showing diminution in size of shadow.

Fig. 2. Shows high position of gall bladder, with flattened appearance of fundus.

negative. Blood pressure 120/80. Morning sickness during first six months.

Cholecystographic findings, May 20, 1927: Gall bladder visualized, degree of concentration +++, globular shape. Fundus ½ inch from middle of first lumbar vertebra and 7¾ inches above the crest of ilium. Normal Boyden meal response. The buttocks of the fetus approximated the fundus of the gall bladder.

Normal delivery and child, July 13, 1927.

Case No. 3, V. B., eighth month of pregnancy. Age 19, weight 140 pounds, height 64 inches. Urine and Wassermann negative. Blood pressure 122/80. No morning sickness during entire pregnancy.

Cholecystographic findings, September 10, 1927: Gall bladder visualized, degree of concentration ++++, shape not unusual. Fundus 2 inches from lower border of second lumbar vertebra and 3¼ inches above the crest of ilium. Normal Boyden meal response. The buttocks of the fetus approximated the fundus of the gall bladder.

Not delivered.

Case No. 5, A. N., eight and one-half months pregnancy. Age 18, weight 125 pounds, height 64 inches. Urine and Wassermann negative. Blood pressure 120/80. Morning sickness during first three months.

Cholecystographic findings, May 13, 1927: Gall bladder visualized, degree of concentration +++, oval shape. Fundus 3¼ inches from middle of first lumbar vertebra and 7½ inches above the crest of ilium. Normal Boyden meal response. The buttocks of the fetus approximated the fundus of the gall bladder.

Normal delivery and child, June 1, 1927.

Case No. 6, A. B., sixth month of pregnancy. Age 18, weight 127 pounds, height 62 inches. Urine and Wassermann negative. Blood pressure 120/80. No morning sickness during entire course of pregnancy.

Cholecystographic findings, April 29, 1927: Gall bladder visualized, degree of concentration +++, flattened appearance. On first exposure, fundus was 3¼ inches from upper border of second lumbar vertebra and 6⅜ inches above the crest of ilium. Normal Boyden meal response. The buttocks of the fetus approximated the fundus

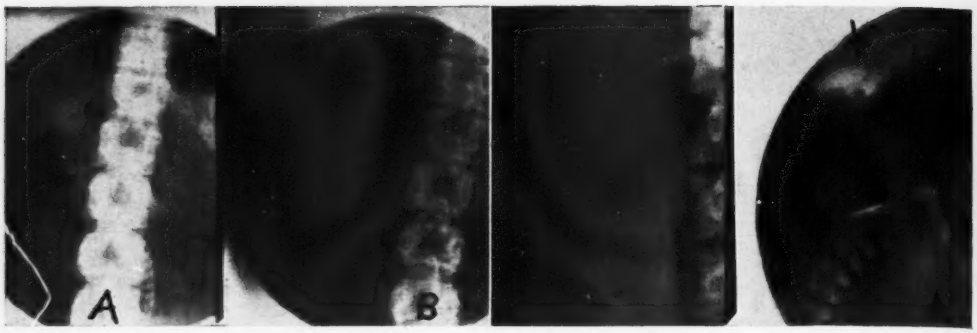

Fig. 3. (*A*) Small, globular, elevated gall bladder. (*B*) Normal Boyden response after one hour.

Fig. 4. (*A*) Gall bladder displaced upward and outward to the right. Note irregularity of contour and flattening of fundus. (*B*) Disappearance of shadow one and one-half hours after Boyden meal.

of the gall bladder. On third exposure, one-half hour later, the head of the fetus occupied previous position of buttocks.

High forceps delivery and normal child, July 4, 1927.

Case No. 9, D. H., eighth month of pregnancy. Age 20, weight 119 pounds, height 60 inches. Urine and Wassermann negative. Blood pressure 130/70. Nausea and vomiting first three months.

Cholecystographic findings, August 31, 1927: Gall bladder visualized, degree of concentration +++, irregular in shape. Fundus 2¼ inches from second lumbar vertebra and 6¾ inches above the crest of ilium. Normal Boyden meal response. The buttocks of the fetus did not approximate the fundus.

Not delivered.

Case No. 10, K. C., six and one-half months pregnancy. Age 23, weight 122 pounds, height 63 inches. Urine and Wassermann negative. Blood pressure 120/70. No morning sickness.

Cholecystographic findings, September 10, 1927: Gall bladder visualized, degree of concentration ++++, deformed, due to pressure. Fundus 1½ inches from upper border of third lumbar vertebra and 3¾ inches above the crest of ilium. Normal Boyden meal response. The buttocks of the fetus did not approximate the fundus of the gall bladder.

Not delivered.

Case No. 12, M. H., eighth month of pregnancy. Age 22, weight 122 pounds, height 64 inches. Urine and Wassermann negative. Blood pressure 120/80. No morning sickness during entire course of pregnancy.

Cholecystographic findings, March 18, 1927: Gall bladder visualized, degree of concentration ++++, assumed elongated cigar shape. Distinct evidence of pressure. Fundus 4¾ inches from middle of second lumbar vertebra and 6¼ inches above the highest point of iliac crest. Normal Boyden meal response. The buttocks of the fetus approximated the fundus of the gall bladder.

Normal delivery and child, five weeks prematurely.

Case No. 13, F. H., seventh month of pregnancy. Age 17, weight 145 pounds, height 64 inches. Urine and Wassermann negative. Blood pressure 115/80. Morning sickness first and second months of pregnancy.

Cholecystographic findings, February 10, 1927: Gall bladder visualized, degree of

Fig. 5. (*A*) Gall bladder irregular in contour, elevated in position, displaced outward to the right. (B) Normal Boyden response at end of one hour.

Fig. 6. Showing relationship of gall bladder to fetal parts.

concentration ++++, shape not unusual. Fundus 2⅛ inches distant from lower third of second lumbar vertebra and 5¼ inches above crest of ilium. Normal Boyden meal response. The buttocks of the fetus did not approximate the fundus of the gall bladder.

Normal delivery and child, April 14, 1927.

Case No. 14, I. W., seventh month of pregnancy. Age 20, weight 136 pounds, height 62½ inches. Urine and Wassermann negative. Blood pressure 115/70. No morning sickness during entire course of pregnancy.

Cholecystographic findings, March 18, 1927: Gall bladder visualized, degree of concentration ++++. On three exposures during the period of one hour, the size and position of the gall bladder varied markedly. The fetus did not change its position. On the first film, the gall bladder was flattened and pushed upward, doorknob-like in shape, the fundus 1¾ inches distant from the upper border of the second lumbar vertebra and 6 inches above the crest of ilium. On the second exposure, the fundus was 3⅜ inches distant from the lower border of the second lumbar vertebra and 4½ inches above crest and had assumed a cigar-shaped appearance. Normal Boyden meal response. The buttocks of the fetus approximated the fundus of the gall bladder.

Normal delivery and child, May 10, 1927.

Non-visualized Group

Case No. 17, N. S., sixth month of pregnancy. Age 17, weight 153 pounds, height 61 inches. Urine and Wassermann negative. Blood pressure 150/100. Morning sickness during first two months.

Cholecystographic findings, April 29, 1927: Gall bladder not visualized. All fetal parts distant from gall bladder and liver region.

Normal delivery and child, July 29, 1927.

Case No. 4, G. H., eighth month of pregnancy. Age 21, weight 170 pounds, height 63 inches. Urine and Wassermann negative. Morning sickness during first and second months of pregnancy.

Cholecystographic findings, July 10, 1927: Gall bladder not visualized. Buttocks well up in region occupied by liver and gall bladder.

Normal delivery and child, July 14, 1927.

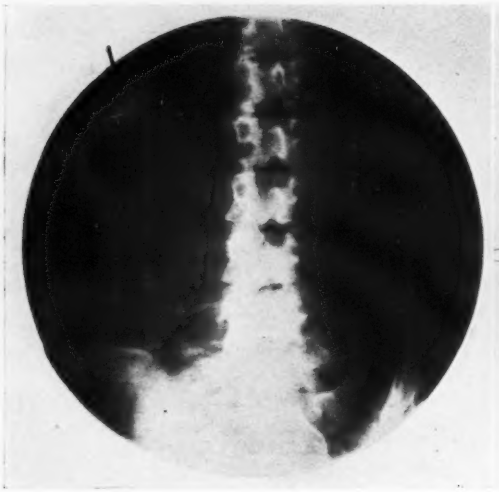

Fig. 7. Gall bladder elevated and somewhat flattened; displaced outward to the right.

Fig. 8. Gall bladder high in position; displaced outward.

Case No. 7, M. P., eighth month of pregnancy. Age 18, weight 125 pounds, height 64 inches. Urine and Wassermann negative. Blood pressure 115/75. No morning sickness during entire course of pregnancy.

Cholecystographic findings, June 10, 1927: Gall bladder not visualized. Buttocks approximate the region occupied by liver and gall bladder.

Normal delivery and child, July 19, 1927.

Case No. 8, E. S., eighth month of pregnancy. Age 18, weight 161 pounds, height 64 inches. Urine negative. Wassermann ++++. Blood pressure 120/80. No morning sickness during entire course of pregnancy.

Cholecystographic findings, August 24, 1927: Gall bladder not visualized. Buttocks approximate the region occupied by liver and gall bladder.

Patient discharged without having been delivered.

Case No. 11, M. S., seventh month of pregnancy. Age 21, weight 121 pounds, height 63 inches. Urine and Wassermann negative. Blood pressure 128/64. Morning sickness during first three months.

Cholecystographic findings, March 25, 1927: Gall bladder not visualized. Buttocks in region of gall bladder.

Normal delivery and child, May 12, 1927.

Case No. 15, M. F., seventh month of pregnancy. Age 17, weight 101 pounds, height 56 inches. Urine and Wassermann negative. Blood pressure 110/70. Morning sickness all during pregnancy.

Cholecystographic findings, February 18, 1927: Gall bladder not visualized. Buttocks in gall-bladder region.

Normal delivery and child, April 1, 1927.

Case No. 16, R. S., seventh month of pregnancy. Age 18, weight 137 pounds, height 60 inches. Urine and Wassermann negative. Blood pressure 138/78. Morning sickness during first three months.

Cholecystographic findings, January 27, 1927: Gall bladder not visualized. Buttocks in region of gall bladder.

Normal delivery and child, March 21, 1927.

CONCLUSIONS

1. In seventeen primiparæ, the intravenous injection of tetraiodo produced no harmful effect on the mother, fetus, or the course of the pregnancy.

2. It is a noteworthy observation that seven gall bladders failed to visualize in a group of otherwise normal women.

3. Ten cases visualized in which concentration of the dye and Boyden meal response were normal.

4. In all of these cases, the gall bladder occupied a high position in the abdominal cavity. In six of the cases, pressure defects were demonstrable.

5. We do not believe that the shadow failures in seven cases were due to mere pressure of the enlarging uterus.

6. It would seem advisable that during the entire course of the pregnancy a properly balanced fatty meal be taken daily to stimulate emptying of the gall bladder and prevent stagnation of the bile with cholesterol precipitation and possible stone formation. It is our opinion that biliary tract disease in pregnant women is of metabolic origin rather than due to the effects of mechanical pressure.

7. Morning sickness occurred more frequently in the series which did not visualize. We realized the desirability of re-examining these cases following delivery for comparative studies, but owing to the fact that the patients were temporary inmates in a public institution from which they were discharged as soon as expedient, it was impossible to conduct subsequent examinations.

We desire to express our gratitude to Professor Francis C. Goldsborough, of the School of Medicine of the University of Buffalo, and to the personnel of the Ingleside Home for their hearty co-operation.

CONCLUSIONS BASED UPON THE ROUTINE INTRAVENOUS ADMINISTRATION OF SODIUM TETRAIODOPHENOLPHTHALEIN IN GALL-BLADDER DIAGNOSIS[1]

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INASMUCH as there are so many fads and fancies that come and go in the practice of medicine from time to time, it is proper for us to pause and check over any new method we are using to see whether we are giving it its proper value and whether it is entitled to retain its place permanently in our work.

A new and particularly a radical method of diagnosis should at least be able to pass the following inquiries:

1. Were our previous methods satisfactory?

2. Is the new method accurate or does it add to the accuracy of our previous methods?

3. Is it free of danger, or, if it is not, is the danger of its administration so slight that it is more than offset by the lessening of the danger in submitting the patient to exploratory or needless operations?

4. Can it be routinely applied?

Before the discovery of radio-opaque substances by Graham and Cole our methods of making gall-bladder diagnoses depended on, (1) direct signs, *(a)* visualization of the pathologic gall bladder, *(b)* visualization of gallstones; (2) indirect pressure signs on the surrounding viscera seen in the administration of a barium meal, and (3) history and physical examination.

The visualization of a pathological gall bladder in the absence of gallstones is such a rare occurrence, if all questionable cases are excluded, as to be of little use. It probably does not occur more than once or twice in a hundred cases of pathologic gall bladder. Gallstones, if there is lime present in them, can be seen without difficulty by any technic that approaches the proper one within reasonable closeness, and all questionable results should be discarded. Indirect pressure signs, if at all plain or characteristic, can be relied upon in making a diagnosis of gall-bladder pathology. Definite gallstone colic, to a careful observer, is diagnostic. Many gallstones do not give symptoms.

The great field of uncertainty in pre-opaque visualization days included gall bladders containing stones which were not radio-opaque, and the cases of cholecystitis—often advanced—which had not produced adhesions or pressure indentation on the adjacent viscera. Furthermore, we had no means of approximating the amount of damage done to the gall bladder except in cases in which stones were visualized.

Like most radiologists who have spent much time in the diagnosis of gastro-intestinal and gall-bladder disease we had become fairly expert in making a gall-bladder diagnosis by taking a careful history, making a physical examination, and watching carefully for gallstones in our films and carefully analyzing indirect pressure signs on the surrounding viscera. In spite of this, physicians and surgeons were quite skeptical about the X-ray diagnosis of gall-bladder disease. The former still relied on their histories, and the latter on their exploratory incisions.

The oral method has never appealed to us because of the numerous sources of error inherent in the method. If a gall bladder

[1]Presented before the Radiological Society of North America at the Thirteenth Annual Meeting, at New Orleans, Dec. 1, 1927.

fills normally by the oral method and empties completely after the second meal, there is no question but that it is a normal gall bladder. The sources of error are vomiting, diarrhea, failure of the patient in following directions in taking the dye, insolubility of the dye, delay or failure in dissolving the capsules or the coating of the dye, uncertainty or unevenness in absorption, or inability of the intestines to absorb the dye, together with the length of time necessary in getting the dye into the circulation. These errors vitiate any conclusions based upon the gall bladder not visualizing, or delay, incomplete filling or emptying of the gall bladder.

The discomfort and reactions of the two methods are about equal. Several patients to whom we have administered the dye by the intravenous method, after having previously given it by the oral method, have stated that they prefer the intravenous method.

We have given sodium tetraiodophenolphthalein intravenously or orally as a routine office procedure for two years and three months, during which time we have administered it about 400 times.

The reactions due to the intravenous administration of sodium tetraiodophenolphthalein are not anaphylactic in type. They are caused by the contraction of involuntary muscle tissue. The reaction is due to the phenolphthalein present in the dye. Precisely the same reaction is produced when phenolphthalein is given intravenously. Occasionally there is a transitory flushing of the face, a feeling of fullness in the head, headaches, and slight dizziness which comes on usually at the time of administration, commonly lasting but a few minutes. Formerly we administered adrenalin min. V. hypodermically when this occurred but we do not now consider it necessary. Vomiting, diarrhea, and uterine cramps may occur, but last only a short time. In women, if given near the menstrual period, the dye is likely to bring on menstruation, and it should not be given to a pregnant woman. If the patient is subject to gallstone colic, it may bring on an attack. Chilliness may occur, which is probably a vasomotor or an involuntary muscle phenomenon. It has no effect on the heart, as shown by the electrocardiograph, but we believe it should not be used when auricular fibrillation is present. We have seen a few cases of rapid heart. The effect on blood pressure is negligible. Covering a period of 2 years and 3 months, with a series of about 400 cases, we have had one alarming reaction.

The oral method produces the same reactions and is especially likely to cause nausea, vomiting, and diarrhea. Usually the deep therapy light or hot applications are all that are necessary to stop the cramps, but occasionally we give codein hypodermically. The reactions are often distressing but never dangerous. We have given it often in the aged (70 to 75 years), and also in high blood pressure cases.

It should not be given to a pregnant woman either orally or intravenously. We believe it is useless in the presence of jaundice. The only case that gave us uneasiness was a man who became practically pulseless shortly after we gave it to him. He was an osteopath and laughed at our uneasiness and stated that he often became pulseless on slight exertion. He was normal the next day.

Our greatest objection to the method is the danger of a local phlebitis at the point of injection in the vein of the arm. We do not believe this occurs so often when the vein on the outside of the arm is injected. When phlebitis occurs we treat it with diathermia.

The directions for preparing the solution are as follows:

METHOD OF PREPARING INTRAVENOUS SODIUM TETRAIODOPHENOLPHTHALEIN SOLUTION AS PREPARED IN THE LABORATORY OF CAREY DRUG DISPENSARY, DENVER: WILLIAM C. PEFFER, R.P.

Material Needed for Preparation

2 2 ounce funnels.
1 2 ounce graduate.
1 125 c.c. glass-stoppered bottle.
1 60 c.c. glass-stoppered bottle.
1 6 inch glass stirring rod.
2 15 cm. Whatman filter papers.
2 250 c.c. Erlenmeyer flasks.
500 c.c. fresh double-distilled water.

METHOD OF PROCEDURE

Fold the filter papers, and place in the funnels.

Prepare in one of the flasks, 250 c.c. salt solution. (Two P., D. & Co.'s normal salt solution tablets dissolved.)

Cover the flask with a small beaker. (Do not use cotton or gauze as the fibers are dissolved by sterilizing.)

Fill the other flask with the double-distilled water, and cover as above.

Place all the materials in an autoclave, or steam sterilizer, and sterilize for 30 minutes, at 30 pounds pressure.

Remove from sterilizer. Measure 60 c.c. of the sterile double-distilled water into the graduate. Dissolve 3.5 grams of sodium tetraiodophenolphthalein by gently stirring with glass rod.

Filter into the 60 c.c. bottle, after washing the filter and bottle with the remaining portion of the sterile double-distilled water.

Wash the filter and bottle with a small portion of the normal salt solution. Filter the balance into the 125 c.c. bottle.

Cork immediately.

The excess of water and normal salt solution is used to wash the filter papers and bottle, and this must be done to wash the condensed steam which collects in the bottles on sterilizing.

The double-distilled water must be freshly distilled.

Our method of administering is as follows:

The patient is instructed to come to the office at 9 A. M. We tell him to take a mild cathartic pill (as Hinkle's, etc.) the night before, or an enema. No breakfast.

1. The patient's arm is cleansed and sterilized.

2. A catheter or rubber tubing is placed around the arm and clamped by a hemostat.

3. Two 30 c.c. glass syringes with No. 22 needles have been sterilized. One is filled with normal salt, the other with 30 c.c. of the solution of sodium tetraiodophenolphthalein.

4. Insert the needle attached to the syringe containing the normal salt. Withdraw a little blood and inject a little normal salt to see if you are surely in the vein. (The escape into the tissue of even a small amount of the solution of the dye is extremely irritating and is apt to cause local necrosis at the point of entry.)

5. Disconnect the normal salt syringe and insert the one containing the dye. Inject the solution very slowly, taking 2 or 3 minutes; disconnect the syringe, leaving the needle in the vein. Refill the syringe with the rest of the dye, and inject the rest of the dye, or, in the case of a very small person, inject in proportion to the body-weight.

6. Disconnect the dye syringe, leaving the needle in the vein, and connect the normal salt. Inject 20 to 30 c.c. of normal salt slowly and withdraw the needle.

7. Disinfect the arm. *Raise the hand in the air for five minutes, contracting the hand several times a minute* in order to flush the vein.

8. If phlebitis occurs, treat it with hot applications or diathermia. This is not a serious condition.

The intravenous injection is given at 9 or 10 A. M., the patient not having had breakfast. We give it routinely in the office. If patients do not have any reaction within an hour, they are sent home. Some go to their routine duties. They are not allowed to eat for 6 hours, but may drink water. At 6 hours a film is taken. They are then sent out to eat a normal meal of solid food. We have never given a meal rich in fats.

We insist on solid food as we believe the pressure of solid food in the antrum and cap against the gall bladder is one of the factors necessary in the normal emptying of the gall bladder. About 2 hours later we take a second film. The patients are directed to eat dinner that night (if they wish it) and also to eat breakfast the next morning. About 9 A. M., 24 hours after injection, a third film is taken. (Preliminary gall-bladder and kidney films, 14 × 17, are always taken for comparison, before the intravenous injection is given.)

The gall bladder does not empty itself if all food is withheld from the stomach. Experimentally the gall bladder can be emptied by giving a meal rich in fats or by giving olive oil intravenously, but these are not the normal methods of emptying the gall bladder. The stools of a patient placed on a milk diet show very little or no bile pigment. Water can be given freely on an empty stomach without emptying the gall bladder. Pituitrin and other preparations which promote peristalsis do not empty the gall bladder unless food is given. Normally the gall bladder empties with a meal of solid food such as one takes three times a day.

Before the gall bladder can empty, we believe that the pressure in the common duct must be raised sufficiently to overcome the sphincter of Oddi. If breathing and intra-abdominal pressure were factors, the bile would dribble continually. There are two factors that can cause increase in pressure in the common duct during digestion:

(1) Secretion of bile, stimulated by the presence of food in the stomach, particularly if the fat content is very high, or by fat or olive oil administered intravenously;

(2) The second factor in increasing the pressure in the common duct is pressure of the antrum and cap upon the gall bladder during peristalsis, if they contain solid food.

Since we have been able to visualize the gall bladder, we find that during active peristalsis the antrum and cap are seen to bulge out and surround the gall bladder. This would undoubtedly increase the pressure in the gall bladder and common duct. When the pressure in the common duct is sufficient to overcome the sphincter of Oddi, the bile will flow out. A fresh cow with a full udder will often drip milk from secretory pressure. The process of milking a cow by hand is quite a similar process to the grasping of the gall bladder by the antrum and cap. For years, a long narrow antrum which did not bulge during peristalsis has been considered suggestive, if not diagnostic, of gall-bladder disease. Pregnancy and great increase in weight would tend to shove the gall bladder away from contact with the antrum and cap. In the sthenic type of individual the gall bladder lies high in the abdomen and farther from the midline than in the average individual, and the antrum is longer and narrower than in the asthenic and medium types, while the cap is very small. The sthenic type is most apt to have gall-bladder pathology. These are the reasons why we believe an average meal of solid food is necessary in the normal emptying of the gall bladder.

INTERPRETATION

If the above technic is used—

(1) A normal gall bladder will fill in 6 hours.

(2) A normal gall bladder will empty one-half to two-thirds in 8 hours.

(3) A normal gall bladder will empty completely after the second meal; a 24-hour film, for the convenience of office routine, is taken at 9 A. M. the second day.

Our routine report is as follows:

An intravenous injection of sodium tetraiodophenolphthalein was given and films taken at 6, 8, and 24 hours.

Six-hour film: Gall bladder visualized or not; of normal density or not.

Eight-hour film: Gall bladder visualized or not; normal density or not; partly emptied or not.

Twenty-four-hour film: Gall bladder visualized or not, and marked density or light density.

If there are abnormalities in size, shape, or position, if negative shadows are seen, or if questionable shadows are made more plain, it is reported.

1. A gall bladder that does not fill by this method (6-, 8-, and 24-hour films) is reported as a non-functioning gall bladder, markedly pathologic gall bladder, or a surgical gall bladder.

2. A gall bladder that does not fill at 6 hours but does fill lightly at 8 hours is also a markedly pathologic gall bladder.

3. A gall bladder that fills normally at 6 hours and empties one-half at 8 hours, but is still plainly visualized at 24 hours is a pathologic gall bladder; the greater the density of the gall-bladder shadow at 24 hours, the more marked the pathology, but not to as marked a degree as the gall bladders in Group 2, *i.e.*, the ones which do not fill readily.

4. Marked distortion of the gall bladder indicates pathology, but the only positive test is whether it does or does not empty after the second meal—the 24-hour film. The 24-hour film is absolutely necessary.

5. A small proportion of low density gallstones may be visualized as negative shadows. However, most gall bladders containing stones are not filled by the intravenous method. Occasionally a gallstone that was imperfectly visualized before the dye was given, may be made quite plain after the dye is administered.

A normal gall bladder should *fill* and *empty after a meal*. If the injection is given at 9 A. M. and the first meal is at 3 P. M., there is not time in an ordinary office or hospital to complete the test, consequently we take one film 2 hours after the patient has eaten and have him return at 9 A. M. the next day. Patients are allowed to eat the evening meal if they wish (most do not), but they are requested to eat breakfast. Even a slight residue seen in the 24-hour negative indicates definite pathology. If there is a definite gall-bladder shadow, it is probably a case of surgical gall bladder.

ANALYSIS OF CASES

We have given the dye, sodium tetraiodophenolphthalein, either intravenously or orally, in a total of about 400 cases, and have been able to classify 360 of these cases, dividing them into groups as follows:

Intravenous Method.—Cases to the number of 285, of which 75 were operated upon. We have divided these into four groups, depending on the radiographic findings with the dye.

Group 1: Those in which the gall bladder did not fill with the dye.

Group 2: Those in which there was decreased density of the gall-bladder shadow at 6 hours and faint or no visualization at all at 24 hours.

Group 3: Those in which the gall-bladder shadow was normal in density at 6 hours and plainly visualized at 24 hours.

Group 4: Those in which the gall bladder filled normally with the dye in 6 hours, was one-half to two-thirds empty at 8 hours (after the first meal), and empty at 24 hours (after the second meal).

Group 1. 76 Cases

This group includes all the gall-bladder cases that did not fill with the dye and are classified by us as non-functioning or surgical gall bladders.

Eight showed stones at 6, 8, and 24 hours; 2 were operated on and stones found; 5 of the 8 were given meals, 4 showing irregular caps and one a normal cap.

Sixty-eight of this group were diagnosed as non-functioning or surgical gall bladders; 30 were operated upon; of these, 18 had stones and 12 chronic cholecystitis of marked degree. Of the 30 operated on, 22 had meals; 18 showed cap deformity. Of the remaining 38 not operated on, 30 were given meals; 25 showed cap deformity.

Group 1 included 76 cases, 8 diagnosed cholelithiasis, 68 non-functioning or surgical gall bladders. Of the 32 operated on, 20 had cholelithiasis; 12 marked chronic cholecystitis. Eighty-two per cent of the cases operated on that were given meals had cap deformity.

Group 2. 98 Cases

This group includes the gall bladders that were markedly decreased in density at 6 hours and faintly or not visualized at all at 24 hours, classified by us as chronic cholecystitis, unless stones were visualized.

In 5, the gall bladder was faintly visualized at 6, 8, and 24 hours, with mottling or negative shadows; diagnosed cholelithiasis.

Two were operated on and stones found.

Four were given meals and the caps found irregular.

Five showed a faint gall-bladder shadow at 6 hours, negative shadows at 8 hours, and not visualized at 24 hours; these were diagnosed cholelithiasis.

Two were operated on and stones found. Both had irregular caps.

Six showed irregular gall-bladder shadows, markedly decreased in density at 6 hours; diagnosed chronic cholecystitis.

Four were operated on; 2 had chronic cholecystitis with adhesions; 2 had chronic cholecystitis. All had irregular caps after the barium meal.

The remaining 82 of this group were diagnosed chronic cholecystitis. Thirteen were operated on, of which 9 had chronic cholecystitis, 3 cases the surgeon said were normal, and 1 was not examined. Of the 3 cases said to be normal, 2 had irregular caps and the gall bladder visualized faintly at 6 and 24 hours. The surgeon said the gall bladders could be emptied manually. One case had an irregular cap; the gall bladder faintly visualized at 6 and 24 hours. The surgeon said there was no pathology of the gall bladder but that there were adhesions around the cystic duct. One was not examined on account of urgent pelvic pathology that had to be corrected.

Of the 9 proven chronic cholecystitis cases, 7, at operation, had irregular caps, with the barium meal.

Of the remaining 69 cases in this group that were not operated on, 55 showed irregular caps, 6 had normal caps, and 8 were not given meals.

Group 2 included 98 cases, of which 10 were diagnosed cholelithiasis, 88 chronic cholecystitis. Of the 21 cases operated on, 4 were proven cholelithiasis, diagnosed by us as such; 13 chronic cholecystitis; 3 said by the surgeon to be normal, and 1 not examined.

Group 3. 50 Cases

This group includes the gall bladders that filled normally at 6 hours, that is, were normal in size, shape, and density, and were plainly visualized at 24 hours. We classify these as cases of marked chronic cholecystitis.

Thirteen were operated on; 12 had chronic cholecystitis, 1 the surgeon said was normal. The one said to be normal had a markedly irregular cap after the barium meal and the gall-bladder shadow was still plainly visualized at 30 hours. Of the 12 proven to have chronic cholecystitis, 9 had meals and showed irregular caps.

Thirty-seven were not operated on. Twenty-five were given meals; 18 had irregular caps and 7 normal caps.

Group 3 included 50 cases diagnosed chronic cholecystitis, of which 13 were operated upon and chronic cholecystitis found in 12; 1 the surgeon said was normal.

Group 4. 60 Cases

This group includes all the cases we interpret as normal gall bladders, that is, they fill at 6 hours, are normal in size, shape, and density, are one-half to two-thirds empty at 8 hours (after the first meal), and entirely empty at 24 hours (after the second meal).

Forty-three were given meals; 14 had irregular caps, 10 of which were diagnosed duodenal ulcers. In the remainder the caps were normal. Nine were operated upon for ulcer or appendicitis and the gall bladder found to be normal in every case.

Group 4 included 60 cases, of which 9 were operated on and the gall bladder found to be normal in all.

Oral Method.—This method includes 75 cases, of which 13 were operated upon. These are divided into four classes, as follows:

Group 1: Those in which the gall bladder did not fill. Non-functioning or surgical gall bladders.

Group 2: Those in which the gall-bladder shadow was of decreased density at 16 hours, slightly or not visualized at 40 hours. These do not fill readily and are diagnosed as chronic cholecystitis, unless stones are visualized.

Group 3: Those in which the gall bladder was plainly visualized at 16 and 40 hours. This group fills readily but does not empty readily; diagnosed as chronic cholecystitis.

Group 4: Those in which the gall bladder was plainly visualized at 16 hours, and empty at 40 hours. These are normal cases.

Group 1. 22 Cases

These include the cases in which no dye or capsules were seen in the colon and neither excessive vomiting nor diarrhea was present after the capsules were given.

Four had dye or capsules in the colon and no diagnosis was given.

One, stones visualized at 16 hours; cap irregular; diagnosed cholelithiasis. (Correct at operation.)

Seventeen diagnosed as non-functioning or surgical gall bladders.

Two were operated upon and stones found; caps irregular.

One was operated upon; chronic cholecystitis; cap irregular.

Of the 14 remaining, 11 were given meals; 4 had normal caps; 7 had irregular caps.

Of this group of 22 cases, 4 were operated upon; 3 had stones; 1 cholecystitis.

Group 2. 21 Cases

These include the cases in which no dye was seen in the colon and no vomiting or diarrhea occurred. The gall bladder was decreased in density at 16 hours, and slightly or not visualized at all at 40 hours. These are interpreted by us as chronic cholecystitis, unless stones are visualized. There is difficulty in filling.

In 2, stones were visualized at 16 and 20 hours; irregular cap in one; neither case was operated on.

Nineteen showed cholecystitis; 3 had irregular gall bladders.

Of the 19, 4 were operated upon, diagnosis correct. Fifteen were given meals; 11 had irregular caps; 4 had normal caps.

Group 2 included 21 cases, of which 4 were operated upon; diagnosis correct.

Group 3. 15 Cases

These include the gall bladders plainly visualized at 16 and 40 hours, all diagnosed chronic cholecystitis. They filled but did not empty readily.

Four were operated upon, chronic cholecystitis found; 3 had irregular caps; 1 normal cap.

Of the 11 not operated upon, 8 meals were given; 2 had normal caps; 6 had irregular caps.

Group 3 included 15 cases, of which 4 were operated upon. Diagnosis correct.

Group 4. 16 Cases

These include the gall bladders filled at 16 hours, one-half to two-thirds empty at 20 hours (after first meal) and empty at 40 hours. These are normal gall bladders.

Ten were given meals; 3 had irregular caps, of which 2 were duodenal ulcers; 7 had normal caps.

One was operated on for appendicitis; gall bladder normal.

COMMENTS

Group 1. Intravenous. Contains the non-functioning or surgical gall bladders in which little or no dye enters. About two-thirds contain stones, the rest are extremely pathologic gall bladders.

Group 2. Intravenous. Contains the low density gall bladders. (Low density at 6 hours, lightly visualized at 24 hours.) Unless stones are actually visualized in the low density group, they have not been found in our cases which have gone to operation. Cholecystitis is found from moderate to marked degree.

Group 3. Intravenous. In this group the gall bladder is of normal density at 6 hours, and of the same density at 24 hours, although generally smaller. No stones were found at operation in any of this group. There is generally a marked cholecystitis.

Group 4. Intravenous. Contains normal gall bladders; that is, they fill at 6 hours, are half empty at 8 hours, and entirely empty at 24 hours. No pathology was found in any of the 9 cases of this group which were operated upon for other conditions.

Indirect pressure signs, principally irregular duodenal caps, or a flattened crescentic indentation on the antrum or cap were seen in about three-fourths of the cases diagnosed as pathologic gall bladders and in about the same percentage that were operated upon.

From a diagnostic standpoint we could group our results as follows:

1. Cholelithiasis. All cases in which either positive or negative stones are shown after the dye method.

2. All cases in which the gall bladder is not visualized (non-functioning or surgical gall bladders). About two-thirds will contain stones. The rest show marked pathology.

3. All cases which visualize at 6 hours, either normal or light in density, which are still visualized at 24 hours, either normal or light in density. These can be safely diagnosed as cholecystitis without stones, if none have been demonstrated in the routine films taken. In other words, if stones are present, either negative or positive, they will be shown in all gall bladders that fill, according to our records.

ANALYSIS OF GALLSTONE CASES DIAGNOSED BY THE DYE METHOD

1. Gallstones visualized after the intravenous method which were not visualized before: (*a*) Positive stones whose density has been increased by absorbing a small portion of the dye—8, Group 1. (*b*) Negative stones outlined by a small portion of dye entering the gall bladder and surrounding the stones of low density—10, Group 2. In this group, in which there is marked obstruction to filling, indicated by a light density gall bladder, there were 5 cases in which the gall bladder was visualized all through

the examination, with mottling or negative shadows. In addition, 5 cases showed a faint gall-bladder shadow at 6 hours, negative shadows at 8 hours, and not visualized at 24 hours. In no case in this group, in which stones were not visualized in the films, were stones proven at operation.

2. Gallstones found at operation excluding gallstones visualized by the dye. These were found in Group 1, the non-functioning gall bladders. In 18 out of 30 that were operated upon, of Group 1, the non-functioning gall bladders contained stones which were not visualized at any time.

3. Gallstones were not found in any case of Group 3, Intravenous Method. This group includes the gall bladders that filled normally at 6 hours, and were plainly visualized at 24 hours.

4. Gallstones visualized after oral method, which were not visualized before. Positive stones in Group 2—one; negative—none. In Group 1, Oral Method, 2 stones were visualized at 16 and 20 hours.

SUMMARY OF INTRAVENOUS CASES

Number of cases examined intravenously 285		Number of cases operated upon 75
Group 1	76	20 cholelithiasis 12 chronic cholecystitis
Group 2	98	4 cholelithiasis 13 cholecystitis 3 normal
Group 3	50	1 not examined 12 cholecystitis 1 normal
Group 4	60	9 normal
	284	75

In addition, one case was given the dye intravenously after the gall bladder had been removed, lateral negatives showing shadows in the hepatic duct. Case operated upon and one stone found at junction of hepatic and common ducts.

SUMMARY OF ORAL CASES

Number of cases examined orally 75		Number of cases operated upon 13
Group 1	22	3 cholelithiasis 1 chronic cholecystitis
Group 2	21	4 chronic cholecystitis
Group 3	15	4 chronic cholecystitis
Group 4	16	1 normal
	75	13

Group 1. Non-functioning or surgical gall bladders; did not fill with the dye; 76 cases.

Diagnosis		Operative findings	Barium meal given	
Chronic cholecystitis 68	Operated on 30	Stones 18 Cholecystitis 12	22	Deformed cap 18 Normal cap 4
	Not operated on 38		30	Deformed cap 25 Normal cap 5
Cholelithiasis 8	Operated on 2	Stones 2	5	Deformed cap 4 Normal cap 1
	Not operated on 6			

Thirty-two cases were operated upon; 20 had stones; 12 marked cholecystitis. Eighty-two per cent of the cases operated upon that were given meals had cap deformity.

One case was given the capsules after the gall bladder had been removed; lateral negatives showed no stones.

In an analysis of the cases, the diagnoses given in the oral method seem to be as good as those given with the intravenous method. However, the diagnoses with the oral method were arrived at by not only using the dye, but by combining the results of this method with the indirect signs obtained with the barium meal, the history, and the clinical findings, and in several cases no diagnosis was given. In about one-half of the cases, the patient was advised to return for a further study with the intravenous method. Furthermore, the intravenous

Group 2. Pathologic light density gall bladders; density decreased at 6 hours; faintly or not visualized at 24 hours; 98 cases.

Diagnosis		Operative findings	Barium meal given	
Cholecystitis 88	Operated on 17	Cholecystitis 13 Normal 4	13	Deformed cap 11 Normal cap 2
	Not operated on 71		63	Deformed cap 57 Normal cap 6
	Operated on 4	Stones 4	4	Deformed cap 4
Cholelithiasis 10	Not operated on 6			

Twenty-one cases were operated upon; no stones found except those shown by X-ray. Eighty-eight per cent of the cases operated upon that were given meals had cap deformity.

Group 3. Pathologic normal density gall bladders; fill normally in 6 hours but do not empty in 24 hours. There is no difficulty in filling but there is difficulty in emptying. Fifty cases.

Diagnosis		Operative findings	Barium meal given	
Cholecystitis 50	Operated on 13	Cholecystitis 12 Normal 1	9	Deformed cap 9
	Not operated on 37		25	Deformed cap 18 Normal cap 7

Thirteen cases were operated on. No stones were found. One hundred per cent of the cases operated upon that were given meals had cap deformity.

Group 4. Fill and empty normally. Sixty cases.

Diagnosis		Operative findings	Barium meal given	
Normal gall bladder	Operated on for ulcer, etc., 9	Normal gall bladder 9	43	Deformed cap 14 Normal cap 29

Nine cases were operated upon for duodenal ulcer or appendicitis. Gall bladders were found to be normal.

group includes several cases examined by the oral method in other clinics, in which the gall bladder was said to be normal and found with the intravenous method to be definitely pathologic.

Since beginning this article one of the cases reported negative on palpation by the surgeon and upon which he refused to investigate the gall bladder further for pathology, has been sent to us with the return of the patient's symptoms. The surgeon has made the statement that he is sorry he did not remove the gall bladder according to our advice, and has requested us to make another test, stating that if the results are the same as at the previous examination, he will re-operate and remove the gall bladder.

CONCLUSION

We find after the routine use of sodium tetraiodophenolphthalein, administered in office practice over a period of 2 years and 3 months, that it is safe, is extremely accurate in estimating the amount of pathology present, and is received with favor by the patient, physician, and surgeon. We consider the intravenous method of Graham and Cole the greatest advance in diagnosis that has been given to the medical profession in years.

DISCUSSION

DR. SHERWOOD MOORE (St. Louis): I wish first to commend this method of holding a symposium on a subject such as this: it is a splendid arrangement. The wealth of material here is so great and good that one scarcely knows how to open the discussion, nor where to begin.

I count myself quite fortunate in having heard the report of Dr. Silverman's work. I think he is going to give us some valuable information on the physiology of the biliary tract.

Next to Dr. Hirsch, I was most entertained by what Dr. Kirklin had to say. It is sometimes regarded as a point against cholecystography that, with apparently normal cholecystograms, the gall bladder is found buried in adhesions. I have encountered that several times, that is, found a functionally normal but widely adherent organ. I believe that this means merely that at some previous time there has been a localized peritonitis with involvement of the serous coat of the gall bladder only. Whether such an organ is normal or not cannot yet be said, but patients with such an organ do have relief after removal of the gall bladder. Dr. Kirklin covered this in a very thorough and comprehensive manner and his statements were most interesting. These procedures, as Dr. Hirsch said, are not going to be 100 per cent, because nothing is 100 per cent in medicine, and I don't imagine that cholecystography is an exception to the rule.

The work of Dr. Skinner and Dr. Lockwood on myocardial changes and infec-

tious arthritis is very important and will be productive of much good, as it has proven to be of great value to us.

Dr. McCoy's paper was most interesting, especially so to one who has just covered the historical aspects of the radiology of the biliary tract, in the last few months. However, I shall have to call his attention to one little error, in ascribing the first work on radiology of the biliary tract to Beck. Beck was preceded by Buxbaum, of Karlsbad, by two years.

Dr. Levyn's paper, read by Dr. Nichols, was very interesting from the standpoint of cholecystography in the late months of pregnancy. We have had 28 such cases, and have found that the procedure is perfectly safe with the intravenous method, both in pregnancy and during the puerperium. We were led into this in an attempt to discover what we might as to the variation in the function of the gall bladder in the pregnant and non-pregnant states. The gall bladder is often seen to be apparently distorted. However, I doubt whether this is more than distortion due to dislocation of a normal organ by pressure of the uterus and its contents.

I profited, as I always do, from anything that comes from Dr. Newcomer. He makes one or two statements with which I would disagree: one as to the deposit of dye on gallstones, which Dr. Case has already mentioned, and the other in regard to the risk of giving cholecystographic dyes to pregnant women.

I do not know what to say in regard to Dr. Hirsch. His paper was, to say the least, interesting. Dr. Case has done about all that could be done with figures; so I have the impression that I am loath to be guilty of quoting any statistics in future. [Laughter.] Dr. Hirsch needs to brush up a little bit on the pathology of the gall bladder and as to what all this cholecystography business is about. Being on the receiving end of some of his *spleen*, I should like to congratulate him on the appropriateness of his title, "Gall and Gall Bladder." [Laughter.]

Dr. Daniel N. Silverman (closing): I simply want to say that I think it would be best if we could have some standard meal for cholecystography, just as we use standard meals in other parts of the intestinal tract in determining function.

Dr. B. R. Kirklin (closing): My reason for selecting the subject, "Normal Cholecystographic Response," was not to criticize the method, but, on the other hand, merely to show its limitations in my hands. I had not intended to discuss the relative merits of the intravenous and oral methods, but, in view of the fact that the subject has been discussed in a very positive manner by one or two of the essayists, I should like to go on record as being somewhat prejudiced to the oral method for two or three reasons. In the first place, it is much simpler and easier to give and entails less risk to the patient for general use. In the second place, it is not necessary to hospitalize the patient, which lessens the responsibility of the examiner and therefore the expense to the patient. Thirdly, it is my opinion that the results are at least within 1 or 2 per cent as reliable with the oral method as with the intravenous. If one will carefully check the accuracy as reported by various observers with both methods, it will be found that there is very little difference. I am at the present time checking a large series of cases with the intravenous administration of the dyes in patients who have previously been examined with the oral method.

As usual, I thoroughly enjoyed listening to Dr. Hirsch's paper. It is true that the statistics can be very misleading. In order to properly evaluate them it is necessary to know exactly what type or group of patients or conditions has been studied and exactly

how the statistics have been computed. It is the only way that I know by which we can determine the merits of any diagnostic procedure.

As the physiologist, pathologist, and surgeon learn more of the relation of gall-bladder physiology and function to gall-bladder pathology, we shall be able to be of still greater assistance to them in making a diagnosis of cholecystic disease.

Dr. C. C. McCoy (closing): As Dr. Moore stated, Buxbaum demonstrated gallstones in the living prior to Beck. Insofar as we can ascertain, this report received but scant recognition and has had practically no influence on the development of the roentgenologic examination of the gall bladder.

Dr. C. A. Conyers (closing): I will answer the questions asked: (1) "Was the barium meal given at the same time as the dye?" In a few cases we gave the meal 6 hours after the intravenous injection, that is, after the 6-hour gall-bladder film had been taken. This is not usually our custom, as we prefer giving the barium meal a few days before or the day following the injection of the dye as the shadow of the barium is liable to overlap the gall-bladder shadow, especially when the 24-hour film is taken.

2. "Do we give the dye to a pregnant woman?" We do not give it in cases of pregnancy as we have had several women menstruate quite freely fifteen to twenty minutes after taking the dye, and quite a number have had severe uterine cramps following the injection. We feel that it may cause an abortion, in case the woman has severe cramps or bleeding.

3. "Do we give the dye to patients with heart disease?" We have had no untoward results with patients having heart disease, but we do not give it to patients with auricular fibrillation.

Dr. I. Seth Hirsch (closing): It is apparent that our paper has started something. The only way we can ever arrive at an accurate estimate of the value of any method is through just such study and discussion as we have had here this afternoon. We must lay aside personal feeling in entering into such a discussion. We must analyze the facts cruelly, critically, and coldly. If cholecystography is to be of general practical utility, it must be by means of the oral method of administration of the drug. If the method is of value only when the examination is made intravenously, I am sure it will never have a general application and never be of great general practical use.

Dr. Case's studies with reference to calculi are very impressive and only bear out what I stated definitely, that the great advantage of cholecystography is that it has increased the percentage of calculi detectable. I am in complete accord with him on this point. In the demonstration of the value of a method or of any particular test, there are certain essentials which must be borne in mind:

Firstly, the technic of the method must be standardized, and those passing judgment on the method must use a similar technic.

Secondly, the cardinal points on which the diagnosis is based must be definitely determined. Later results may modify the verdict as to the value of the particular points, but the criteria on which the diagnosis is based must be definitely understood.

Thirdly, the determination of the correctness or incorrectness of the diagnostic criteria must be checked by the pathologic findings and there must be an agreement as to these pathologic findings.

Scanning the literature, it will be found that not one of these essentials is observed. There is no established technic; there are certainly no definite data as to what roentgen signs signify a pathologic gall bladder

and pathologists are not agreed as to what constitutes real pathologic gall-bladder changes—particularly in the early stages, and the statistics are certainly of no value in that they are not founded on similar criteria, and conclusions and percentages are drawn and compiled on too few cases.

I want earnestly to state that my attitude is not one of carping criticism. My purpose is merely to stimulate more careful study. I am extremely sympathetic to the method, but time has yet to show its exact value. Just now it is not the only and most valuable method of determining gall-bladder pathology. We are progressing in the direction of accurate gall-bladder disease diagnosis, but whether we are moving along correct lines in basing our sole hopes on the present cholecystographic method, I am not as yet prepared to admit.

Dr. James T. Case, Battle Creek, Mich. (closing): I believe this has been a very profitable discussion. We have heard discussions on various aspects of the cholecystographic problem—proponents of the oral method and of the intravenous method; advocates of the so-called indirect method and opponents of that method. We have seen reports of statistical studies of long series of cases and of short series. We have heard from one of our distinguished New York members that the radiological study of the gall bladder, even with the added help of cholecystography, has increased very little or none at all the accuracy of diagnosis of gall-bladder lesions.

I desire to emphasize at this point the fact that the statistical reports cited here to-day have one serious fault, namely, that they are built up on cases which went to surgery for a supposed gall-bladder lesion. This very fact indicates that the statistics are faulty, for only those cases came to surgical check which were characterized by sufficient clinical evidence of gall-bladder disease to warrant surgical operation; and it is safe to say that the surgeons would not have operated unless there had been other evidence of biliary tract disease besides that furnished by cholecystography. This gives such statistics a bias of which the radiologist, perhaps quite unconsciously, has taken advantage, for it unquestionably boosts his percentage of correct diagnoses. To be quite fair, it would be necessary to check his positive findings controlled by operation by an equal number of negative findings controlled by operation.

Since this latter suggestion (control of a large number of negative findings by operative observation) is hardly likely to be feasible, it has occurred to me that I might usefully present before you some statistics of my own work, which include an analysis of a rather large number of cases with negative findings, and another series of nearly one hundred cases in which we have interpreted the findings of Graham's test by the intravenous method as indicating a pathologic gall bladder without stone.

I have recommended the following terminology for use in reporting the findings of the Graham test: (1) *"Stone Positive,"* referring to those cases where the presence of stones is confirmed by cholecystography. Naturally, if the stone contains enough lime to cast a characteristic shadow without the use of the dye test, one makes the report on the direct finding. In the case of cholesterin stones, or where the shadow is very faint or of unusual shape or in an unusual position, the dye test is needed to demonstrate the identity of the stones. (2) *"Absence of Shadow,"* which has a very definite and grave significance when the test is given intravenously. (3) *"Normal,"* when the gall-bladder outline appears with normal contours, of normal uniform density, without filling defects, and emptying within the normal time, having nearly, if not completely, evacuated the dye within three hours follow-

ing the ingestion of a fatty meal. (4) *"Pathological, Non-calculous,"* including all cases not falling under one of the three headings just listed. It naturally includes those cases where the shadow is faulty in density or in uniformity, or where the contours are irregular, or a combination of these abnormalities. This, again, is a finding which is more likely to be reliable when the test is given intravenously. However, all the foregoing classifications are applicable to the oral method, and I earnestly recommend them for your consideration in the hope that you will adopt these four phases ("stone positive," "absence of shadow," "normal," "pathological, non-calculous") in your own work, so that the reports we make shall be mutually understandable.

The following tabulations show the results of operative check in nearly three hundred consecutive cases which have come to surgery in our clinic:

"Stone Positive."—Total number of cases operated on, 77; stones found at operation in 74; errors, 3; percentage error, 3.9 per cent; reliability, 96.1 per cent; errors in first series of 46 cases, 3; in second series of 31 cases, 0.

"Absence of Shadow."—Total number of cases operated on, 79; stones found present in 58 cases (73.4 per cent); no stones found, but gall bladder grossly pathological, 21, or 26.6 per cent; errors (normal at operation), 2, or 2.5 per cent; reliability in finding gross disease of the biliary tract, 97.5 per cent.

An analysis of the 21 non-calculous cases where "absence of shadow" was reported, showed carcinoma of the pancreas or common duct in 5; abscess of the liver in 1; cirrhosis of the liver in 2; chronic pericholecystitis, with adhesions, especially about the gall-bladder neck, in 5; papillomatous gall bladder in 1; chronic cholecystitis, fibrosis of the walls, with thick, tarry black bile, 5, and the cause of absence of shadow not apparent, normal bile being found in the gall bladder, in 2.

"Absence of shadow" (by the intravenous method, at least) therefore signifies gross disease of the biliary tract, with only 2.5 per cent probability of error. In 73.4 per cent of cases, stones were found at operation; in 87.3 per cent of cases, gross disease, either stones or other pathology, in the gall bladder itself; in 10.1 per cent, gross disease of the biliary system outside of the gall bladder.

"Normal."—Of 36 cases checked at operation, 4 were considered pathological but without stone and were not removed; 22 more were considered normal and left in place; 10 were removed on account of the history, and, of these, 3 were considered as mildly pathologic by Dr. Warthin. Thus, of 36 cases which came to operation, with a pre-operative interpretation of Graham's test as "normal," 7 were thought by the surgeon to be mildly diseased. There is thus a percentage of 19 per cent error with the "normals." It should be emphasized that in none of the cases reported as "normal" was a stone found; it seems clear, therefore, that the negative or "normal" Graham test by the intravenous method, and probably also by the oral method, should raise very serious doubt about the advisability of surgery.

"Pathological, Non-calculous."—Of 85 cases checked at operation, the gall bladder was found to be pathologic in 14 cases, 6 of them showing gallstones. In these six cases the stones were very small. For the exclusion of gallstones this report, therefore, values 93 per cent; toward the finding of a pathologic gall bladder without stone, 83.6 per cent.

This is the group in which we naturally would find the greatest difficulty in making a perfectly reliable report. In some instances the gall bladder might be non-calculous, yet pathological to a mild or fairly ex-

tensive degree; in others, it might be calculous, but not so very much interfered with as to function. We have adopted the plan of expressing the degree to which we think the reports warrant a statement that pathology is present by using a numeral after the report, *e.g.*, "pathological, non-calculous No. 2," on a basis of 1 to 4, the latter representing the most extensive grade of pathologic change. This scheme has turned out to be fairly satisfactory, when compared with operative findings.

In reviewing the value of Graham's test, by the intravenous method, in our hands, toward excluding cholelithiasis, we found that in 121 cases in which we had made a pre-operative report after cholecystography of "Normal" in 36 cases, and "Pathological, Non-calculous" in 85, the operation revealed stones in 6, an error of 4.9 per cent. On the other hand, in 138 cases which came to operation where stones were found by the surgeon, in our pre-operative Graham test we had reported "Absence of Shadow" in 58, "Stone Positive" in 74, and "Pathological, Non-calculous" in 6, or an error of only 4.3 per cent. This tabulation shows that with an error of less than 5 per cent we were able to report either a "Stone Positive" or "Absence of Shadow" in 132 out of 138 cases.

It is, therefore, evident that in 95 per cent of cases of cholelithiasis, one at least of the following decisive X-ray signs should be present: (1) Stones visible by direct X-ray examination without resort to Graham's test, such stones containing sufficient lime to make positive shadows; (2) Stones visible by negative areas in the cholecystographic shadow; (3) Failure of the gall bladder to visualize after Graham's test by the intravenous method.

In adjourning this symposium, permit me to thank the gentlemen who have contributed to its success. I hope that next year's Program Committee will see fit to continue the effort to put on at least one half-day session in a similar manner, and that the participants in such a symposium will have their papers in the hands of the editor in time for publication in advance of the meeting.

Owing to lack of space in this issue two papers belonging to this symposium, *Routine Cholecystography, with Report of 625 Cases*, by W. Warner Watkins, M.D., and Harlan P. Mills, M.D., and *Results of the Oral Method in Cholecystography*, by Joseph Aspray, M.D., will be published in the next issue of RADIOLOGY.

QUALITY DETERMINATION OF THE ROENTGEN RAYS[1]

By WILLIAM H. MEYER, M.D., and CARL B. BRAESTRUP, B.Sc., Department of Roentgenology New York Post-graduate Medical School and Hospital

THE recent interest created by the introduction of a standard unit of measuring the intensity of the roentgen rays again brings to the forefront the importance of creating a uniform method of quality determination. Our interest in the matter has been expressed in former communications and herewith we present the results of our continued experimentation along these lines.

(1) THE HALF VALUE LAYER AS A PREFERENTIAL QUALITY MEASURE

The adoption of a single method for determining and expressing the quality appears to us to be just as important as the acceptance of a standard unit of intensity.

The first part of our present work consisted of the comparison of several of the more recently proposed methods for measuring the quality.

In Chart I we have tabulated our experimental results. The arrangement is such that the relative advantages of each method can easily be determined. An important point not evident on the chart is the practical difficulty encountered with some of the methods. This is especially true where an absorbing medium of high atomic number is employed in measuring the rays of long wave length. We have reference to the handling of fine thicknesses of metal requiring micrometric measurements below one-tenth millimeter (Method B, Chart I), as well as to the difficulties presented in measuring small quantities of transmitted intensity (C, E, and F).

The percentage of variation of the transmitted intensity with the shorter wave length is very small as applied in Method E.

From the foregoing it is evident that heavier absorbing mediums, suitable for testing strongly filtered rays, offer serious difficulties in measuring rays of long wave length. Conversely, fixed lighter absorbing mediums give too narrow a range with rays of short wave length.

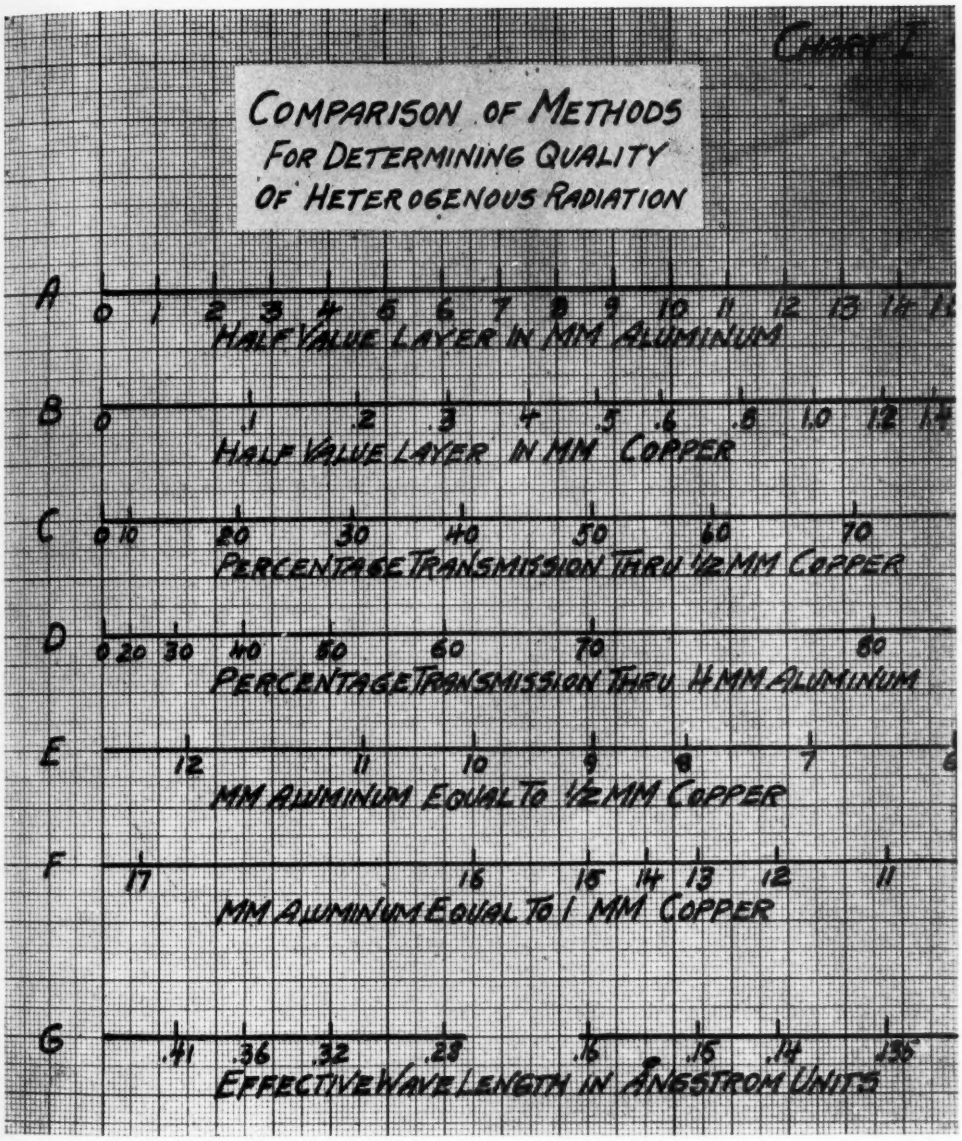
Further, it may be worthy of mention that in existing tables the number of Ångström units are indicated with homogeneous radiation (1). On the other hand, the practical roentgen therapist is mostly dealing with a heterogeneous beam. Therefore rather wide variations occur, depending upon the method employed, as indicated in Scales E and F compared with the effective wave length given in G.

A further study of the chart reveals the fact that the half value method, especially with aluminum, can be used over the full range of wave lengths with the least number of the objections heretofore mentioned. The determination of the half value layer in copper with the rays of shorter wave length has certain scientific advantages; there is, however, either the difficulty of handling extremely thin layers (as previously mentioned) or the necessity of substituting another medium for measuring the soft rays, thus introducing a double standard.

The advantages of using the half value layer in aluminum as a quality measure appear to be:

1. The thickness of the absorbing medium is quite *proportional to the quality.*
2. But a *single absorbing medium* is ap-

[1]Submitted for publication April 16, 1928.



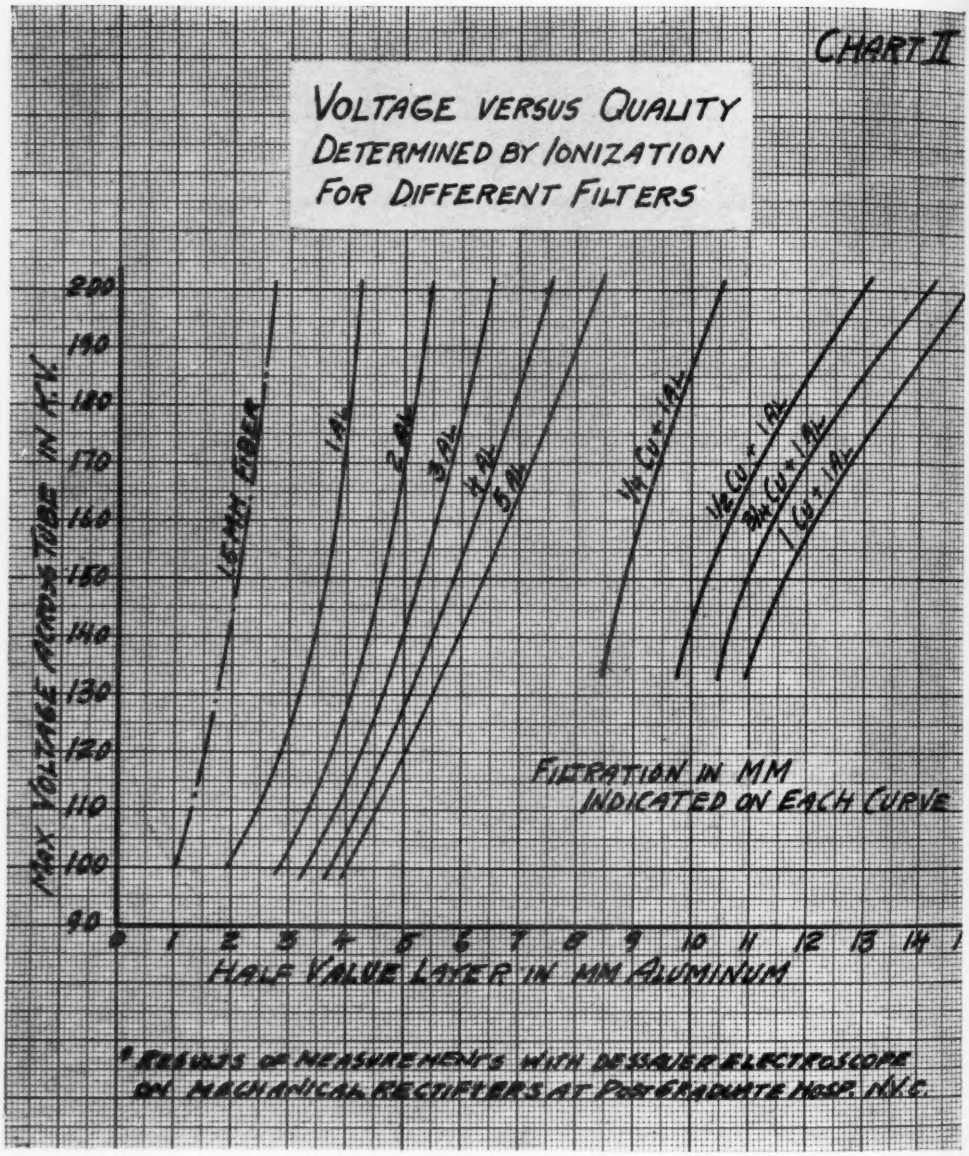
plied throughout the full range of wave lengths.

3. *Simplicity of statement,* with a single unit standard, *avoiding transposition.*

4. The method is reasonably *simple* of application and appears to afford the greatest *accuracy* over the widest range.

(2) THE RELATION OF THE HALF VALUE LAYER TO SOME OF THE PRACTICAL OPERATING CONDITIONS IN ROENTGEN THERAPY

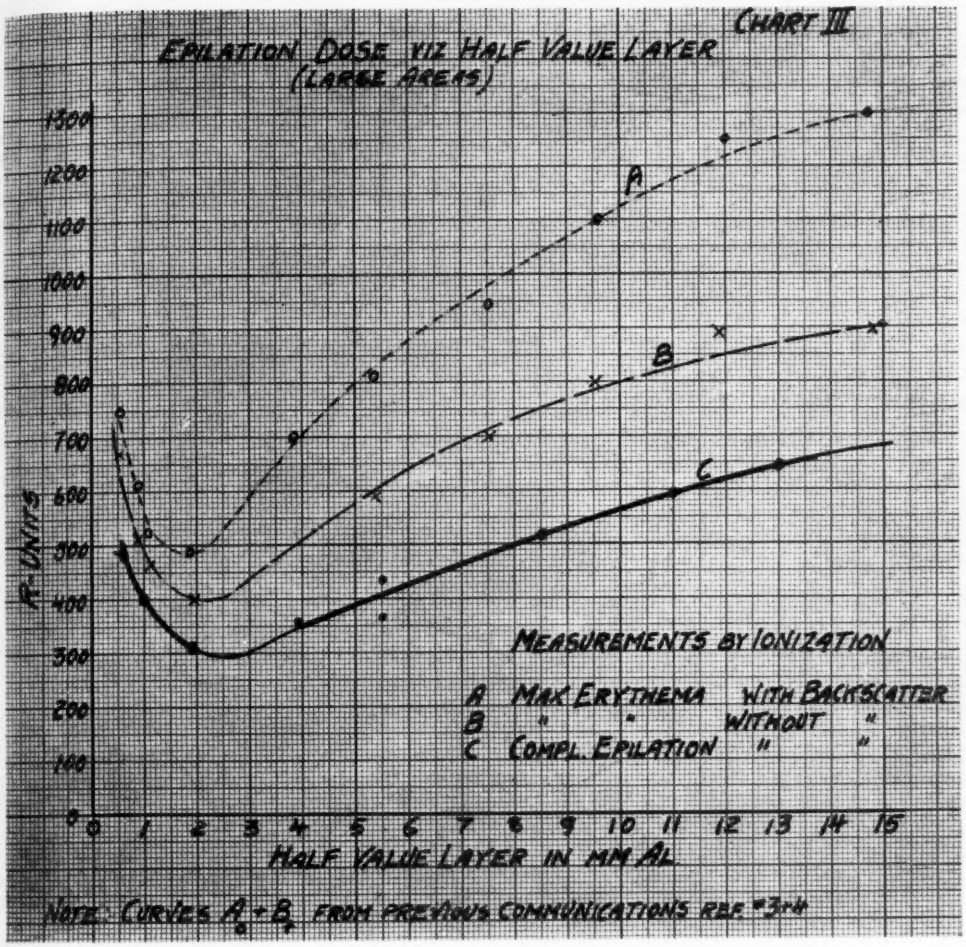
In Chart II are shown in graphic form the results of half value determinations



with the mechanical rectifiers in this department. While the findings may differ slightly with other installations, the curves give a general idea of the quality one can expect, using various voltages and filtrations.

With such types of apparatus where parallel gaps are not supplied or where the use of a sphere gap is not advisable, the chart makes it possible to check the manufacturer's settings of the machine. In this way the operator can establish a clear conception of the quality output on any installation as compared with previous acquired knowledge or other data.

A study of the chart further shows the



effect of voltage as well as filtration on the quality. It indicates the advantage of copper over aluminum as a filter for the higher voltages. It shows again that the half value layer in aluminum covers a very wide range for quality determination, thereby affording a fair degree of accuracy throughout the scale of wave lengths.

Since the year 1914 we have been using the half value layer in aluminum as a quality measure (2). Formerly we relied upon the photographic method in making these measurements. During the past three years, however, the greater accuracy afforded by ionization has been supplemented. The continued use of a single method of quality determination renders possible quite accurate back reference to all of our previous work. We herewith append a table showing the comparative half value measurements by the ionometric and photometric methods of determination with the various voltages and filtrations as here employed.

It will be noted that the values obtained by the photographic method compare very closely with the ionization measurements when filtered rays are employed. We have, however, found a wider variation when

measuring rays of long wave length, the ionization method always giving a lower figure than when photographically determined. This is especially true when unfiltered rays are employed.

(3) FURTHER STUDIES OF THE INFLUENCE OF RADIATION QUALITY ON BIOLOGICAL OR SKIN REACTION

In the accompanying Chart III we have drawn another curve (C) showing the relation of physically measured quality and quantity to a given biological reaction. The cases used in drawing this curve were selected from current material in the Therapy Department, as illustrated in Table 2. Those cases in which a complete epilation over reasonably large areas followed by complete re-growth of hair are listed. The *R*-units were established without back-scattering, using standardized Wulf ionometers. The quality determinations were made with the Dessauer Electroscope. To afford closer comparison, curves A and B (drawn in dotted lines) are transcribed from previous communications (3) (4).

TABLE 1

K.V. Peak	Filter in mm.	Half value layer in mm. Aluminum	
		Photographic (Rough)	Ionization[2] (Absolute)
45	1½ Fiber	¾ +	0.65
—75	1½ Fiber	1 +	0.8
+100	1½ Fiber	1½ +	1.
+135	1½ Fiber	2	1¾[3]
+135	2½ Al.	4 +	4½
+135	4½ Al.	6 —	5½
+135	¼ Cu.	9 —	8½
+135	½ Cu.	11—	11+
200	¾ Cu.	14 +	14½

The experimental data of the (gross) *photographic* half value layer in relation to the absolute half value layer determination by *ionization.*

[2]Ionization measurements with Dessauer Electroscope.
[3]Less than 0.2 variations not recorded.

It is evident from our last curve (C) that the percentage variation of the number of *R*-units required with the different ray qualities is not as great as when a full erythema dose is used (Curve B); or when the intensity measurements are made directly on the patient or a phantom (Curve A).

Curve C again demonstrates a considerable variation of the number of *R*-units when producing similar biological reactions with varying ray qualities (5). In other words, from a given point, especially noticeable with increasing filter thickness, the number of *R*-units necessary to produce similar reactions increases with an increasing half value layer.

That the curve with respect to the number of *R*-units will again rise when using soft and unfiltered rays is not alone illustrated by our former experiments but seems confirmed by the fact that with the so-called super-soft rays no epilation occurs even in the face of sharp erythema reactions (6).

It is quite likely that erythema reactions of varying degrees may be obtainable over a wide range of wave lengths with practically the same number of *R*-units. This is more likely true when the exposed areas are small and the comparative intensity measurements are made in air (7) (8)

TABLE 2

Diagnosis	No. of cases. 1 Series	No. of areas. Total	Half value layer (d½) in mm. Al. Photogr.	*R*-units *Average* in round figures
Ringworm scalp	77	411	1½	400
Favis scalp	1 1	5 5	1 3	500 —
Sycosis, Tinea barbæ	23	75	1½	400
Furunculosis cerv. and occip.	15	36	6	440
Furunculosis axillary	1 4 2	1 4 2	1 6 9	500 360 500
Dermatitis papil. cap.	1 2	2 9	2 4—	— 350
Brain tumor Child Child Adult Adult	1 4 12 1	3 16 55 5	6 9 11— 13—	400 Aver. 500 600 650

The type and number of cases as well as the number of areas in which complete epilation was produced. Each area was included within a 5-inch cone. In each instance complete re-growth of hair occurred.

The quality and quantity are recorded in half value layer in Al. and *R*-units, respectively. These data form the basis for the curve drawn in Chart III.

(9). Our work, on the other hand, has been accomplished with large areas whereon a complete epilation was followed by complete re-growth of hair, it being our opinion that such a determination is a better test of biologic reaction than either incomplete epilation on small areas or a variable range of erythema reactions.

SUMMARY

In the foregoing pages

1. We recommend the determination of the half value layer in aluminum as the best measure of roentgen quality.

2. We have presented data with respect to the practical application of the half value layer.

3. We have shown the influence of ray quality on the epilation dose.

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X-RAY TREATMENT OF BONE TUMORS, WITH SPECIAL REFERENCE TO TUMORS OF UNCONFIRMED DIAGNOSIS[1]

By MAX KAHN, M.D., Baltimore, Maryland

THE object of this communication is to call attention to the fact that, although diagnosis is unconfirmed in a certain group of bone tumors, radiation may produce arrest or healing and the patient remain symptom-free and clinically well for a number of months or years following treatment. It is well to emphasize that surgery in some cases is the method of choice, and we feel that when it is combined with deep radiation in such instances, the results may be improved. The treatment of both benign and malignant bone tumors by deep X-ray is of value. Of the benign tumors, the giant cell tumor appears to have responded well and there have been cases reported with excellent results. In contradistinction to the malignant tumors, pain and swelling are very apt to be increased at first in the treatment of the giant cell tumor, symptoms which may persist for from four to six weeks. About this time both these symptoms begin to subside, and this is followed by recalcification with more or less solidification of the bone shell.

Osteomyelitis and syphilis of bone in our experience do not respond well to deep radiation and are best treated surgically or by other suitable methods.

Of especial interest is the treatment of tumors wherein the diagnosis is unconfirmed by biopsy. The difficulty in the surgical treatment of tumors involving the skull, shoulder, pelvis, hip joints, and spine is manifest, and this difficulty is increased when there is at the same time considerable infiltration of the surrounding soft structures. It is not unusual for such tumors to have the X-ray and clinical appearance of malignancy, with the history suggesting malignancy.

Biopsy is apt to stimulate metastasis and increase the rapidity of the growth of these tumors, and in these cases it should perhaps best not be done. From the scientific standpoint biopsy is essential for a correct diagnosis.

From the clinical standpoint the results from deep radiation are sometimes excellent, and, as mentioned before, the patient may remain clinically well and symptom-free for a number of months or years. Some tumors treated with deep X-ray respond quickly, namely, there is lessening of pain and regression of the tumor and the surrounding infiltration following the first few treatments.

Sarcoma frequently involves the long bones, and, where practical, amputation or resection offers good results. Prophylactic deep X-ray treatment over the lungs in these cases is strongly advised.

Myxoma, in our experience, does not readily respond to radiation and the results up to the present have been disappointing, although one case appears to have responded fairly well to both deep X-ray and colloidal lead treatments. We have had practically no experience in the treatment of multiple myeloma.

There is no other agent so helpful as the X-ray in carcinomatosis. As a brief illustration, recently a patient presented herself for examination six years following surgical removal of the breast for carcinoma. She had considerable pain in her back and hip joints, difficulty in walking, and was almost bedridden. Roentgenograms revealed destruction of the bones of the pelvis, destruction of some of the ribs, and the beginning

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Nov. 29, 1927.

of destruction in one humerus. She was given a course of deep radiation over the greater part of the skeleton, particularly over the involved regions. Within a few days practically all pain had disappeared and now—about three months later—she has gained some weight, her appetite has improved, and she is able to walk without difficulty. Roentgenograms at this time reveal no increased destruction nor new areas of involvement, and in places there is a tendency to recalcification. It is, of course, too early to tell how lasting the effect of the radiation will be, but, from a hopeless bedridden condition, this patient at present is able to enjoy life reasonably free from pain. She is under observation and will receive radiation from time to time. Other cases of carcinoma, particularly those in which there are only one or two areas of metastasis to the bones, are living from three to four years following deep radiation. In these cases there is a tendency to recalcification and healing of the bone or bones involved.

The following cases are of especial interest.

Case 1. Referred by Dr. Bloodgood in December, 1922. C. McQ., white male, age 16 years. Complains of pain in left scapula and upper end of left humerus, and inability to make much motion at the shoulder joint except a little forward and backward; no abduction. Patient states that about five months ago he fell on the left shoulder. Swelling, which has been present since, has grown larger. Four days after falling he had difficulty in moving his arm, and this difficulty has gradually increased. No marked pain, only tenderness.

Examination by Dr. Bloodgood: Inspection anteriorly shows the affected left shoulder to be lower than the right. There seems to be some swelling anteriorly over the head of the humerus. On palpation anteriorly, one can get a thumb between the end of the acromial process and the head of the humerus on the left side, but not on the right side. The head of the humerus is also much more movable on the left side than on the right. Inspection posteriorly shows the wing of the right scapula to be prominent;

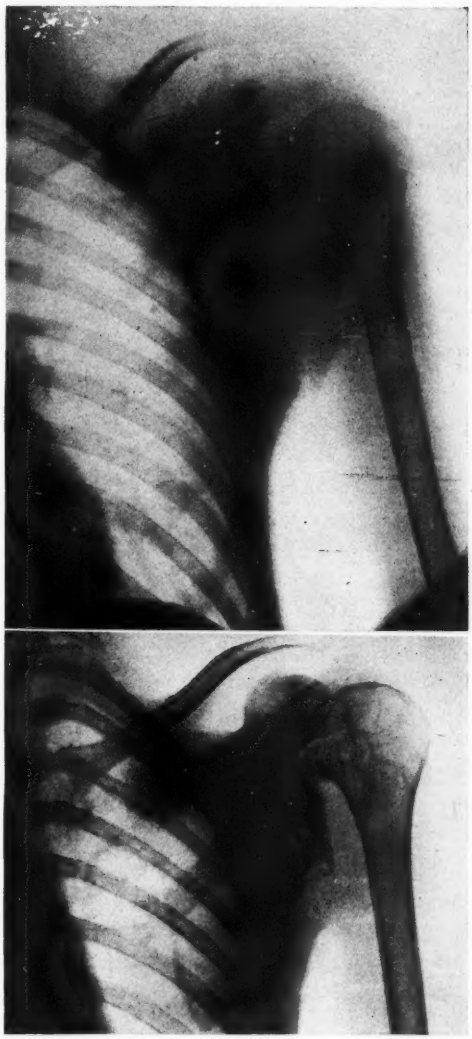

Fig. 1 (above), Case 1. Extensive destruction of scapula, suggesting a malignant bone tumor, with infiltration of neighboring soft structures. Head of humerus dislocated upward.

Fig. 2 (below), Case 1. Five years after deep X-rays treatments. Note reformation of scapula, with areas of absorption in region of glenoid. Head remains dislocated upward, but there is good function. Patient clinically well.

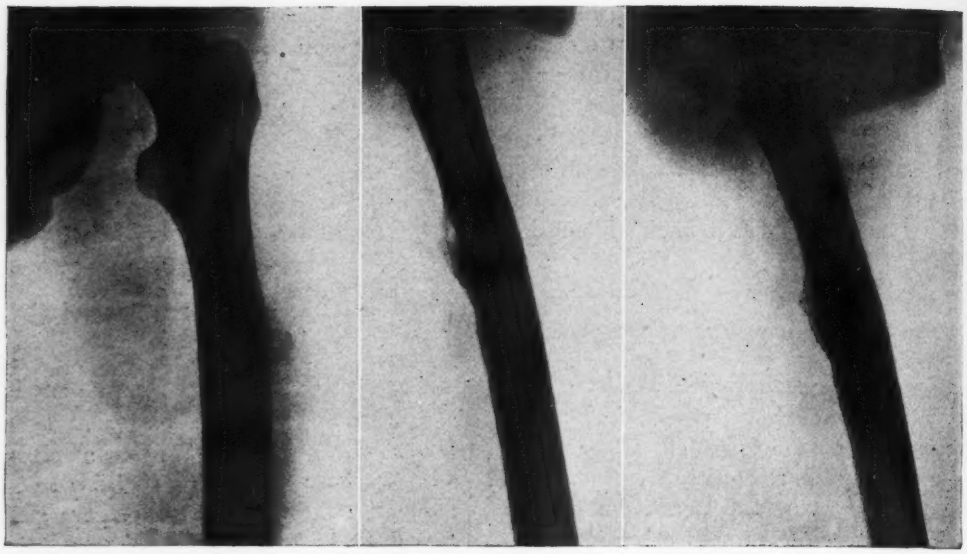

Fig. 3, Case 2. New bone formation with bone destruction along outer and posterior aspect of shaft of femur, suggesting malignancy.

Fig. 4, Case 2. Lateral view of case shown in Figure 3.

Fig. 5, Case 2. Four years after deep X-ray treatments. The new bone is now smooth and suggests healing (cf. Figs. 3 and 4). Patient clinically well.

the wing of the left is not seen. The most marked swelling is below the spine towards the arm. The subscapular fossa is less distinct than on the right. When the arms hang at the side, the scapula becomes visible. On palpation the swelling is chiefly over that portion of the scapula below the spine, beginning about 3 cm. from the edge of the wing. It feels more like edema. Above the spine there is a little thickening of the fossa—less distinct. Below the spine there is marked infiltration of the soft parts. As to passive motion, I can lift the arm from the body only about 45 degrees. There is evidence of infiltration of muscles above and below the spine on the outer half of the scapula, with suggestion of fluid in the joint. The blood examination, including a Wassermann test and test for Bence-Jones bodies, is negative. X-ray examination of the chest is negative. There is no positive evidence of metastasis.

X-ray examination of the left shoulder joint reveals the left scapula to have been practically destroyed due to some lesion which involved it and the surrounding soft structures. Since no biopsy has been made, we cannot say with certainty whether we are dealing with a malignant neoplasm or destruction due to some other cause; whichever it is, the scapula seems to be completely destroyed and there is extensive infiltration of the surrounding soft structures.

This patient received a course of deep X-ray treatments directed over the left scapula and shoulder joint from Jan. 31, 1923, to Aug. 21, 1923. It is now nearly five years since the first treatment. The left scapula has been restored practically to normal in appearance, with the exception of a small area in the lower half of the glenoid, where the loss of bone substance suggests the formation of a large cavity or two. The head of the humerus has been dislocated up-

Fig. 6, Case 3. Destruction due to metastases to left frontal bone and left greater wing of sphenoid three years after amputation of femur for myxosarcoma.

Fig. 7, Case 3. Recalcification of the destructive areas following combined deep X-ray and colloidal lead treatments.

ward from the first and has remained in this upward position ever since. It has formed an artificial joint high up. The head of the humerus reveals some bone atrophy due to slightly impaired function. The patient now is clinically well, has gained weight, and is earning a living in a clerical position. Although the head has formed a new joint he has fairly good use of his arm. Tissue removed from a small area on the arm about 3 cm. below the axilla on April 18, 1924, and examined microscopically by Dr. Bloodgood, revealed highly vascular granulation tissue. There is no evidence of sarcoma. Dr. Bloodgood notes at this time that this granulation tissue has nothing to do with the disease, but suggests an accidental infection.

Case 2. Referred by Dr. Bloodgood, in December, 1923. W. M. O., white male, age 18 years. Trauma to left thigh in football game, November 24, 1923. A slight limp resulted, and two weeks after accident the thigh began to ache, being worse at night. There was no swelling except a little hard spot on the bone. Treatment by an osteopath had been given three weeks after injury, from which the patient says he felt some improvement. Since that time the swelling has grown a little larger. On palpation, a mass is felt at the junction of the upper and middle thirds of the femur. X-ray examination of the left femur reveals a tumor shadow along the outer aspect, about the junction of the upper and middle thirds. There is some new bone formation extending outward into the soft structures and some bone destruction involving the cortex. It is difficult to tell the exact nature of this bone tumor, but it has the appearance of malignancy. Blood examination, including a Wassermann test and a test for Bence-Jones bodies, is negative. X-ray examination of the chest is essentially negative. There is no positive evidence of metastasis.

The patient received a course of deep X-ray treatment from December 31, 1923, to March 10, 1924. It is now about four years

since these X-ray treatments and a restudy of the left femur reveals that the new bone formation is largely absorbed and at the site of the tumor there is now smooth, dense bone suggesting a healed condition. The patient is symptom-free and clinically well at this time.

A note by Dr. Bloodgood, made on his examination of the patient June 23, 1924, states that the periosteal mass on palpation felt distinctly smaller than at the time of the initial examination. There was no question about that, but there was still a periosteal mass, beginning a little below the trochanter and extending to the junction of the middle third, but distinctly smaller. The soft-part tumor which was present when the patient completed treatment had practically disappeared. There was an area of red skin and a sinus corresponding to the point where a rupture had occurred four weeks previously, pus and a piece of bone coming out. The bone has been examined microscopically and reported negative.

Case 3. M. T., white female, age 44 years, single. This patient had a destructive bone tumor of the lower third of the left femur above the condyles in January, 1924. The femur was amputated about the middle third, by Dr. Bloodgood, on January 23, 1924, for myxosarcoma. There was no positive evidence of metastasis to the lungs. The patient was seen at intervals from January, 1924, to November, 1927. An X-ray examination of the head in February, 1927, more than three years after amputation of the femur, revealed destruction of the left frontal bone and left greater wing of the sphenoid, strongly suggestive of metastasis. The chest was negative. She received a number of deep X-ray treatments from February, 1927, to November, 1927, and in addition received colloidal lead treatments from Dr. Henry T. Collenberg, from April, 1927, to October, 1927. An X-ray examination of the head in November, 1927, revealed considerable recalcification of the destructive areas. There was also bulging of the left eye, but, following X-ray treatments and colloidal lead, the bulging became markedly less. Clinically the patient feels well and is able to get about with an artificial leg. It is interesting to note that this case of myxosarcoma, with metastases three years later to the frontal and sphenoidal bones, has responded to combined deep X-ray and colloidal lead.

AMERICAN ASSOCIATION OF RADIOLOGICAL TECHNICIANS

At the annual meeting of the American Association of Radiological Technicians, held in Chicago in April, the following officers were elected for the coming year: *President*, Mrs. E. C. Grierson, Saint Paul, Minnesota; *First vice president*, Eugene R. Corson, Savannah, Georgia; *Second vice president*, E. S. Hoare, Calgary, Alberta, Canada; *Third vice president*, Sister Mary Artos, Milwaukee, Wisconsin; *Secretary*, F. A. Senechal, Saint Louis, Missouri; *Treasurer*, Miss Mary E. Bell, Minneapolis, Minnesota.

Mr. Claude J. Bodle, of Winnipeg, Manitoba, Canada, was appointed chairman of the Publication Committee, which is to have charge of all manuscripts submitted for publication.

EDITORIAL

M. J. Hubeny, M.D. . . . . *Editor*
Benjamin H. Orndoff, M.D.
John D. Camp, M.D. *Associate Editors*

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PRESENT STATUS OF CHOLECYSTOGRAPHY

At the present time the greatest problem in cholecystography seems to be the choice between intravenous and oral methods of administration, and the suitability of the particular drug used, especially in regard to the reaction sustained by the patient. Gradual refinement in interpretation during the past few years has established criteria of diagnosis which in most hands have yielded an accuracy equal to 95 per cent or more. Most of the errors in diagnosis can be attributed to difficulty in determining what degree of decrease in density of the shadow is necessary to constitute a pathological condition, or how much distortion of the shadow is necessary to justify a diagnosis of pericholecystitis. Elimination of a portion of the errors from these sources is to be expected as observation improves our diagnostic criteria, but it is asking too much to expect entire freedom from error. Scarcely any laboratory or clinical procedure exists which can offer an accuracy of 100 per cent in diagnosis.

The choice between the intravenous and oral methods of administration of the substances used in cholecystography appears largely to be a personal one. It is not difficult to understand why some workers would find it inconvenient to resort to the slightly more elaborate technic of intravenous administration. In our experience, the intravenous method yields a higher percentage of accuracy than the oral. The criteria for diagnosis likewise seem more delicate and more subject to error when using the oral method. From a physiological standpoint, the latter method also offers two other sources of error: inconstancy in amount and rate of absorption, and, in a small percentage of cases, possible loss of dye by vomiting or diarrhea. Repetition of the test is more necessary after the oral administration than after the intravenous.

It might be expected, however, that after an individual worker has established his own criteria of diagnosis following the oral administration, and carefully guarded against sources of error, his diagnostic accuracy will be as great as that obtained from the intravenous method. Numerous reports from different workers, submitting a diagnostic accuracy of 93 to 97 per cent with the oral method, have borne out this assumption.

We have observed that the number of patients (68 per cent) free from any toxic symptoms whatever was greater after the intravenous injection of phenoltetraiodophthalein than after the oral administration of tetraiodophenolphthalein (33 per cent). The number of patients sustaining more severe reactions (second degree reactions) in the above series was higher after oral administration of tetraiodophenolphthalein (45 per cent) than after the intravenous administration of phenoltetraiodophthalein (6.5 per cent).

For some reason, possibly because of an increased rate of excretion, the intravenous dose of phenoltetraiodophthalein (2.5 grams) required to produce an adequate shadow of the gall bladder, is not as large as the intravenous dose of tetraiodophe-

nolphthalein. The decreased number of reactions following the intravenous use of phenoltetraiodophthalein has been so striking that we have adopted it for intravenous use instead of tetraiodophenolphthalein. Its only disadvantage is the price. However, the difference in price certainly does not seem sufficient to prevent its substitution for tetraiodophenolphthalein if reactions following the latter have been disagreeable. No advantage of the oral administration of phenoltetraiodophthalein over the oral use of tetraiodophenolphthalein can be made out.

An important advantage of phenoltetraiodophthalein, when given intravenously, over tetraiodophenolphthalein lies in its ability to stain the blood serum, thereby making determinations of hepatic function possible. A recent observation of ours indicated that patients having a high retention of dye were poor surgical risks. This has convinced us that such patients should receive supportive pre-operative treatment, with delay in operation until such time as the hepatic function has attained a safe level. In differential diagnosis between certain diseases, the determination of the dye retention in the blood serum has given a very gratifying accuracy. Especially is this true in differentiating between jaundice arising in carcinoma of the liver and jaundice due to obstruction of the common duct by stone.

The exact value of the fat meal as a diagnostic aid in interpretation of the cholecystographic films has not as yet been determined. Although in our experience we have not been able to obtain a greater percentage of accuracy by employing the fat meal, there seems no doubt that information can be gained from its use which shortens, somewhat, the time necessary for cholecystographic examination.

Considerable dispute has arisen as to the diagnostic value of persistence of a shadow of the gall bladder beyond 24 hours. Earlier in the development of cholecystography it was thought that a delay in emptying of the organ and retardation in disappearance of the shadow indicated an atony of the gall-bladder wall, or possibly disease of the cystic duct, with partial constriction. The experience of Moore and others has not borne out this belief. On numerous occasions persistence of the shadow has been observed when all other characteristics of the series were normal. The explanation probably lies in the fact that the food partaken of during the examination did not contain sufficient fat and protein to produce emptying of the gall bladder, as concluded from the experiences of Whitaker and Boyden. Another factor which undoubtedly causes a persistence of the shadow on numerous occasions is re-absorption of the iodized salt from the intestinal tract, thereby allowing reconcentration in the gall bladder several hours later.

WARREN H. COLE, M.D.

INVITATION TO WIESBADEN

Professor Alban Köhler, of Wiesbaden, Germany, extends a cordial invitation to those attending the International Congress of Radiology to visit the institute, which contains an extensive library and numerous appliances of historical value.

INVITATION TO VISIT ITALY[1]

The Italian radiologists will be very pleased to receive the Americans coming to Italy on their way to Stockholm. I shall be at their disposal in my Instituto, Galleria Umberto 8 (Palazzo Banco d'Italia), Naples, to give all the assistance necessary for visits to the leading radiologists and the most important roentgen and radium institutes in all parts of Italy. I am sure that

[1]This invitation is extended through Dr. G. E. Pfahler, President of the American Committee for the Second International Congress of Radiology.

the Italian trip will be very enjoyable to your countrymen and will be the means of introducing them to the beauties of the country, its art treasures, and the great progress made in the last years.

[Signed] P. TANDOJA, *President,*
Societa Italiana di Radiologia Medica.

A COMMUNICATION

To the Editor of RADIOLOGY
Dear Sir:

You are to be congratulated upon the conception of a "Standardization Number" for RADIOLOGY. Unfortunately certain inaccuracies are occasionally published which should be corrected lest misunderstandings and harm result from the acceptance of such errors as facts. After considerable deliberation, and with hesitancy, I wish to call attention to some errors which are contained in the paper of Dr. Pohle and Dr. Barnes in the current issue of RADIOLOGY (Vol. X, No. 4). My comments are made only with a sincere desire to point out the necessity of extreme caution and accuracy in the publication of deductions from poorly established experimental data. Original investigators may occasionally draw out erroneous conclusions, since there is no precedence whereby to corroborate their work; but in procedures which are made to corroborate or disprove the work of others, one should be very certain that at least physical conditions are as consistent and accurate and based upon as acceptable data as those of the original research.

In the first part of the paper of Dr. Pohle and Dr. Barnes is a description of their experiments to establish again the widely accepted fact that the quality of radiation may be determined and reproduced with accuracy by the absorption in aluminum or copper, that the Duane effective wave length method is acceptable, and that the Meyer photographic method gives satisfactory approximate values. The experimental results of the authors are given in Tables I and II, pp. 303-304. A careful analysis of these tables shows certain inaccuracies and inconsistencies to which I wish to call attention.

That the Duane charts for determining effective wave lengths are not applicable for soft rays is a generally accepted fact. When the authors used soft rays in their experiments they therefore attempted to replace the effective wave length values by the transmission values of 4 mm. of aluminum, but they failed to transfer the transmission values into effective wave lengths, which is possible by readily available data (Richtmyer and Allen). Because of this omission the different terms which the authors use to express the quality of their soft radiation in Table I mean nothing and are misleading. This is seen if we note that the effective wave lengths shown are almost the same, no matter what filter is used. Thus, according to the table, there is little or no difference (0.37 A. to 0.4 A.) between the effective wave lengths when using either 2, 3 or 4 mm. of aluminum at 80 or 90 K.V.; whereas a considerable difference is really obvious in the quality under the conditions enumerated.

In Table II they show two entirely different effective wave lengths for a particular X-ray beam, depending upon whether absorption in copper or aluminum is used. For example, for 110 K.V. and 3 mm. of aluminum the effective wave length is 0.33 A. when measured in aluminum and 0.24 A. when copper is used. Such a large and unexplained difference is unsatisfactory to indicate quality under the conditions of radiation.

The authors continued their experiments to investigate and compare the quality of radiation by use of the half value layer in aluminum and copper by means of the photographic and ionometric methods. Their experimental data are shown in Tables I and

II. Apparently the authors are trying to show the well-known differences which exist between these two methods; however, the data which they have presented are too inconsistent to demonstrate a preference for either method. A superficial survey of these data would indicate that the photographic method gives somewhat higher values than the ionometric method. This result would be expected when soft radiation is used. But a more careful study of the tables shows such great variations that it would really be impossible to come to any such conclusion. A few examples from the data presented will point out the wide range of error.

In the column for 80 K.V. with unfiltered rays (Table I) there is a difference of 208 per cent between the half value layers as measured by the photographic and ionometric methods, but if 1 mm. of aluminum is added the difference drops to only 9 per cent; with 2 mm. of aluminum the difference is 79 per cent, and with 3 mm. it is 44 per cent. Similarly, for 90 K.V. with unfiltered rays the difference is 285 per cent; for 1 mm. of aluminum added it drops to 53 per cent, and with 3 mm. of aluminum it is 25 per cent. The analysis of the data shows that the smallest variation is 7 per cent and the largest is 314 per cent—variations which show their consistent inaccuracy. The authors give no reason for these wide variations but may have expected such results from the photographic method. That this is not the case, however, is shown by further study of the data of the ionometric half value layer method. Here, for example, in Table II, we find that the half value layer in aluminum for 100, 110, and 120 K.V. with unfiltered rays is 0.9 mm. for each, thus showing no increase whatever as the voltage is increased. However, when 130 K.V. is used, a sudden rise of almost 50 per cent to 1.4 mm. is shown and again a surprising drop to 1.3 mm. when voltage is increased to 150 K.V., but a similar irregularity does not appear in their data in the column showing the half value layer in copper; therefore the irregularity previously mentioned can not be due to a peculiarity in their X-ray apparatus.

On the basis of their own data the authors themselves would be unable to arrive at any conclusion as to the actual differences which exist between the photographic and ionometric methods, nor could they determine which method is preferable. If they have accepted their own experiments as a basis for determination of quality in their other investigations, then their observations are not based upon accurate information and are of no value.

In the standardization of a number of X-ray installations the authors state that they have preferred to use the half value layer method in order to determine quality, and their observations are summarized in Tables IV and V. By studying these tables and comparing them with Table II we find that each of these installations, with two exceptions, has given exactly the same half value layer (quality) as their own installation. This would mean that all these installations which they have calibrated must have had the same quality output for the same conditions of voltage and filtration. This is most peculiar since it is universally known that there are very wide variations in both quality and quantity output of different rectified machines even under identical operating conditions. Were it true that X-ray installations are as uniform as the authors indicate, there would be no necessity for trying to discover a satisfactory method for determination of quality, since voltage and filtration alone would be sufficiently accurate.

In the last columns of Tables IV and V data are also given which represent different erythema doses in *R*-units as they have been measured without back-scattering. The au-

thors have called this the "Roentgen Value" of Holthusen, but have misapplied the term since Holthusen defines "Roentgen Value" as "the number of *R*-units per minute which is delivered by the radiation at a focal distance of 30 centimeters and without additional back-scattering." The dose which the authors present is obviously something entirely different from the Roentgen Value of Holthusen.

It would also seem, therefore, that the attempt of the authors to disprove the work of Meyer and Glasser on the differences in the erythema reactions to different wave lengths is not founded upon a sound physical basis. That they should contradict the observations of Meyer and Glasser seems inconsistent, since they attempt to show no variation in erythema reactions with different qualities of radiation; yet they state, "for the present we feel free to recommend the following doses as safe according to our experience (Table VI)." It will be noted in this table that the doses which they recommend vary from 200 *R* with the soft radiation at 60 to 130 K.V., up to 600 *R* with the hard rays of 150 to 200 K.V. This would indicate that they do believe that there is a variation of erythema reactions dependent upon wave length, as was observed by Meyer and Glasser.

The authors refer to the calibration of their Wulf Ionometer in our Research Laboratory by Dr. Glasser. In order to prevent possible misunderstandings and erroneous conclusions being drawn from the inaccuracies of their data on the basis of this calibration, I wish to add a few words. The "R," or "E," unit which was established in our laboratory four years ago has been frequently found to be identical with that of Duane and recently with the *R*-unit of Behnken. Dr. Glasser has made three attempts but has failed completely to calibrate the instrument of the authors, because, in the first attempt, they were using no standard radium control and in two later attempts the leakage of their instrument was too great to make any calibration possible.

Since the methods in use at present for the determination of the quality and quantity of radiation are sufficiently accurate, well recognized, and generally accepted, any further attempt to increase our knowledge of quality and quantity determinations must be established upon a sound physical basis. On account of the inaccuracies of the data given by Dr. Pohle and Dr. Barnes it would seem that they would make roentgenologists suspicious of the dependability of dosage as based upon physical measurements.

At New Orleans so many data were presented in this paper of Dr. Pohle and Dr. Barnes that, unfortunately, it was impossible to analyze or to indicate the errors and inconsistencies in an extemporaneous discussion. After careful study of the data presented, I feel that the question is of sufficient moment to merit attention and criticism, especially at this time when the dosage question is an international problem.

U. V. PORTMANN, M.D.,
Cleveland Clinic,
Cleveland, Ohio.

April 26, 1928

RECEPTION TO AMERICAN LEGION PHYSICIANS

As announced to our members, the reception given the American Physicians who came to France with the American Legion, took place Saturday, September 24, at the Restaurant Le Doyen. About forty of our members answered an announcement and some of them from a distance, to bring our former allies evidence of their affection.

Among our American guests we must mention Dr. Kennon Dunham, of Cincinnati, representing the Rehabilitation Committee of the Legion; Dr. Hamilton, of San Francisco; Dr. Knowles, of Colorado, and

others. And among our American confrères in Paris, Dr. Edmund Gros, and Dr. G. G. Rimbaud, former Director of the Pasteur Institute of New York.

The dinner table was most handsomely decorated in the colors of the two nations, and the banquet was served in excellent style by the Maison Le Doyen.

—From the Bulletin of the Association Amicale des Anciens Medecins des Corps Combattants, Paris, Oct.-Nov., 1927, through the courtesy of Dr. Jacques Forestier, Aix-les-Bains, France.

THE NEXT ANNUAL MEETING

It may not be premature to remind the members of the Society to plan on attending the meeting in December. It falls early enough in the month to avoid conflict with Holiday celebrations, and Chicago in early winter enjoys an excellent character as to weather.

The Drake Hotel, where the sessions and exhibits are all to be held, faces Lake Michigan, and is just far enough from the Loop to avoid the congestion and hurry which have made Chicago famous. It will introduce to many an interesting phase of Chicago. For instance, the new Northwestern University medical center is but a few blocks from the hotel.

Summer view of the Lake Michigan beach. The Drake Hotel is seen on the right. It has formed the nucleus for a new residential and shopping district.

ABSTRACTS OF CURRENT LITERATURE

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Regarding the Method of Choice in Treating Fibroids and Uterine Hemorrhage. C. J. Gauss. Strahlentherapie, 1927, XXVII, 5. Radium Treatment in Non-malignant Diseases of Women. E. Ritter von Seuffert. Strahlentherapie, 1927, XXVII, 81.

These two closely related papers are not suitable for a brief abstract; a few points, however, may be mentioned. Gauss insists that a curettage should be done before treating any uterine hemorrhage or a fibroid, in order to rule out a malignancy. Roentgen rays are usually preferable to radium; it must be admitted, however, that in certain cases radium stops the bleeding more quickly. Seuffert feels that radium is indicated in diabetes or in very fat patients, in women suffering from heart disease, or if the possibility of a pigmentation of the areas treated by roentgen rays is feared by the patient. He also gives tables relating the results and doses of radium treatment in non-malignant conditions in women, compiled from the publications of a number of radiologists.

E. A. POHLE, M.D.

The Diagnosis of Pyloric Ulcer. Frank Novotny. Am. Jour. Roentgenol. and Rad. Ther., August, 1927, XVIII, 130.

The author describes the rather minute anatomical and spastic changes in the prepyloric antrum, pylorus, and at the base of the first portion of the duodenum, whereby he feels that in the majority of cases ulcer pathology is detectable by roentgen examination, with the reservation that the differential diagnosis by X-ray signs alone between ulcer and post-ulcer scarring is often not possible. Indirect signs elsewhere in the stomach are generally very meager or entirely absent, and local tenderness immediately over the ulcer site he does not find to be a reliable sign. A series of sketches showing the changes as seen fluoroscopically, for the exact location of ulcers on or near the pylorus, accompanies the article.

J. E. HABBE, M.D.

Interesting Facts about the Heart: With an Analysis of Cases. Arthur E. Mark. Calif. and Western Med., February, 1928, p. 216.

The author discusses the causative factors in heart disease and then the diagnostic aids, saying, "Additional methods for the determination of cardiac enlargement should supplement auscultatory examination." The X-ray has aided materially in this, and, properly done, the orthocardiogram is by all means the most accurate means. The X-ray, however, should not entirely replace the physical examination.

F. B. SHELDON, M.D.

Bone Tumors. Henry G. Hill and Jarrell Penn. Jour. Tenn. State Med. Assn., January, 1928, p. 301.

Since the most important differentiation to make in bone tumors is between benignity and malignancy, these authors present their discussion in the form of a differential diagnosis of osteogenic sarcoma. Although the entire thickness of the shaft is involved in osteo-

genic sarcoma, it may predominate in one form or another, and the differentiation is considered under the classes of (*a*) periosteal, (*b*) central, and (*c*) diffuse. From periosteal sarcoma must be differentiated ossifying periostitis of traumatic, infectious, and syphilitic origin; benign osteogenic tumors such as exostosis and osteoma, and periosseous fibrosarcoma. The central lesions are considered, according to location, in four classes: those in the distal third or epiphyseal ends in persons under 18 years of age; those in the middle third in persons under 18; those in the epiphyseal ends and in the diaphysis in persons over 18. The diffuse sarcomas are divided into the sclerosing and the osteoporotic. Under the head of treatment, X-ray therapy is mentioned as a minor factor. The article is well illustrated with radiographs.

W. W. Watkins, M.D.

Radiation Therapy in Hyperthyroidism. Albert Soiland, William E. Costolow, and Orville N. Meland. Calif. and Western Med., December, 1927, p. 789.

The authors point out that, in hyperthyroidism, the mortality rate, as estimated by the general surgeons throughout the country, is probably near 12 to 15 per cent. During the past ten years consistent reports of radiologists have shown that results of irradiation are certainly equal to those obtained with surgery. The authors believe that the most important factor in the success of radiation treatment is the proper selection of the patient, and in these selected cases there can be no logical contraindications to radiation treatment.

The severe case of hyperthyroidism should be kept in bed, under the care of a competent internist, using the same routine that the skillful surgeon has used to reduce surgical mortality. The metabolism test is invaluable in this form of treatment. Often at the end of three or four months the rate is normal, but some cases are six months in returning to this condition; therefore, there is no need for discouragement if the reaction appears to be slow. Because of the large number of patients who are treated so easily and effectively, without mortality, the authors believe that this method of treatment should be given first consideration.

F. B. Sheldon, M.D.

Bone Cavities: A Roentgenologic Study. E. Gordon Stoloff. Am. Jour. Roentgenol. and Rad Ther., July, 1927, XVIII, 26.

The many explanations advanced as etiological of bone cysts by numerous writers in the past are described briefly by the author. The conception by Pommer and Looser of their being of hematogenous bone sac origin, or of their being "expansive bone hemorrhages" is the theory accepted by the present writer. Expansive hemorrhagic cysts are classified as solitary (localized) cysts, and multiple (generalized) cysts. Bone cavities not of hemorrhagic cystic origin are of infectious origin, either chronic osteomyelitis, tuberculosis, parasite, or syphilis. Not included under the author's classification of bone cavities, but nevertheless to be considered in the differential diagnosis, are the central tumors, which may be the giant cell tumor, chondroma, myxoma, myeloma, or metastatic carcinoma.

The roentgen findings in chronic inflammatory osteomyelitis, tuberculosis, and syphilis, and also in the slowly progressing central tumors, are described. The article closes with illustrated case reports of expansive hemorrhagic cysts, osteomyelitis, tuberculosis, central sarcoma, and osteochondroma.

J. E. Habbe, M.D.

X-Ray Tubes - - - - Supplies
Equipment
American Vacuum Company
F. R. Eltinge, Manager
1011 Chestnut Street Philadelphia, Pa.